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(71) Applicant: ABBOTT LABORATORIES [US/US]; CHAD 0377/AP6D–2, 100 Abbott Park Road, Abbott Park, IL 60064–3500 (US).

(72) Inventors: BHAGWAT, Shripad, S.; 30055 N. Waukegan Road, Lake Bluff, IL 60044 (US). LEE, Chih–Hung; 966 Dunhill Road, Grayslake, IL 60030 (US). COWART, Marlon, D.; 43 E. Dahlia Lane, Round Lake Beach, IL 60073 (US). MCKIE, Jeffrey; Apartment 211, 716 Water's Edge Drive, Lake Villa, IL 60046 (US). GRILLOT, Anne, Laure; Apartment 2, 99 Hammond Street, Cambridge, MA 02138 (US).

(74) Agents: YANG, Frank, Z. et al.; Abbott Laboratories, CHAD 0377/AP6D–2, 100 Abbott Park Road, Abbott Park, IL 60064–3500 (US).

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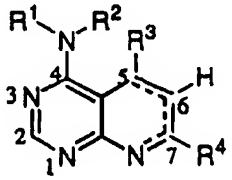

(I)

(57) Abstract

A method for inhibiting adenosine kinase by administering a compound having formula (I) wherein R^1 and R^2 are independently selected from H, loweralkyl, C_1–C_6alkoxyC_1–C_6alkyl, arylC_1–C_6alkyl, –C(O)C_1–C_6alkyl, –C(O)aryl, –C(O)heterocyclic or may join together with the nitrogen to which they are attached to form a 5–7 membered ring optionally containing 1–2 additional heteroatoms selected from O, N or S; R^3 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group, heteroarylalkyl or heterocycloalkyl wherein the heteroaryl and heterocyclic groups are linked directly or indirectly by a ring carbon; R^4 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group heteroarylalkyl or heterocycloalkyl; and a dashed line —— indicates that a double bond is optionally present provided that proper valencies are maintained, a pharmaceutical composition comprising a therapeutically effective amount of a compound thereof above in combination with a pharmaceutically acceptable carrier, and a method of treating cerebral ischemia, epilepsy, nociperception, inflammation and sepsis in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound thereof, a process for preparing said compounds, and compounds having the above formula wherein R^1, R^2, R^3 and R^4 are separately defined.

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5,7-DISUBSTITUTED 4-AMINOPYRIDO[2,3-D]PYRIMIDINE COMPOUNDS AND THEIR USE AS ADENOSINE KINASE INHIBITORS

Technical Field

The present invention relates to a method of inhibiting adenosine kinase by administering 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds, to pharmaceutical compositions containing such compounds, as well as to certain 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds.

Background Of The Invention

Adenosine kinase (ATP:adenosine 5'-phosphotransferase, EC 2.7.1.20) is a ubiquitous enzyme which catalyzes the phosphorylation of adenosine to AMP, using ATP, preferentially, as the phosphate source. Adenosine kinase has broad tissue and species distribution, and has been isolated from yeast, a variety of mammalian sources and certain microorganisms. It has been found to be present in virtually every human tissue assayed including kidney, liver, brain, spleen, placenta and pancreas. Adenosine kinase is a key enzyme in the control of the cellular concentrations of adenosine.

Adenosine is a purine nucleoside that is an intermediate in the pathways of purine nucleotide degradation and salvage. Adenosine also has many important physiologic effects, many of which are mediated through the activation of specific ectocellular receptors, termed P_1 receptors (Burnstock, in *Cell Membrane Receptors for Drugs and Hormones*, 1978, (Bolis and Straub, eds.) Raven, New York, pp. 107-118; Fredholm, *et al.*, *Pharmacol. Rev.* 1994, **46**: 143-156).

In the central nervous system, adenosine inhibits the release of certain neurotransmitters (Corradetti, *et al.*, *Eur. J. Pharmacol.* 1984, **104**: 19-26), stabilizes membrane potential (Rudolphi, *et al.*, *Cerebrovasc. Brain Metab. Rev.* 1992, **4**: 346-360), functions as an endogenous anticonvulsant (Dragunow, *Trends Pharmacol. Sci.* 1986, **7**: 128-130) and may have a role as an endogenous neuroprotective agent (Rudolphi, *et al.*, *Trends Pharmacol. Sci.*, 1992, **13**: 439-445). Adenosine may play a role in several disorders of the central nervous system such as schizophrenia, anxiety, depression and Parkinson's disease. (Williams, M., in *Psychopharmacology: The Fourth Generation of Progress*; Bloom, Kupfer (eds.), Raven Press, New York, 1995, pp 643-655.

Adenosine has also been implicated in modulating transmission in pain pathways in the spinal cord (Sawynok, *et al.*, *Br. J. Pharmacol.*, 1986, **88**: 923-930), and in mediating the analgesic effects of morphine (Sweeney, *et al.*, *J. Pharmacol. Exp. Ther.* 1987, **243**:

657-665). In the immune system, adenosine inhibits certain neutrophil functions and exhibits anti-inflammatory effects (Cronstein, *J. Appl. Physiol.* 1994, **76**: 5-13). An AK inhibitor has been reported to decrease paw swelling in a model of adjuvant arthritis in rats (Firestein, *et.al.*, *Arthritis and Rheumatism*, 1993, **36**, S48.

Adenosine also exerts a variety of effects on the cardiovascular system, including vasodilation, impairment of atrioventricular conduction and endogenous cardioprotection in myocardial ischemia and reperfusion (Mullane and Williams, in *Adenosine and Adenosine Receptors*, 1990 (Williams, ed.) Humana Press, New Jersey, pp. 289-334). The widespread actions of adenosine also include effects on the renal, respiratory, gastrointestinal and reproductive systems, as well as on blood cells and adipocytes. Adenosine, via its A1 receptor activation on adipocytes, plays a role in diabetes by inhibiting lipolysis [Londos, *et al.*, Proc. Natl. Acad. Sci. USA, 1980, **77**, 2551.

Endogenous adenosine release appears to have a role as a natural defense mechanism in various pathophysiologic conditions, including cerebral and myocardial ischemia, seizures, pain, inflammation and sepsis. While adenosine is normally present at low levels in the extracellular space, its release is locally enhanced at the site(s) of excessive cellular activity, trauma or metabolic stress. Once in the extracellular space, adenosine activates specific extracellular receptors to elicit a variety of responses which tend to restore cellular function towards normal (Bruns, *Nucleosides Nucleotides*, 1991, **10**: 931-943; Miller and Hsu, *J. Neurotrauma*, 1992, **9**: S563-S577). Adenosine has a half-life measured in seconds in extracellular fluids (Moser, *et al.*, *Am. J. Physiol.* 1989, **25**: C799-C806), and its endogenous actions are therefore highly localized.

The inhibition of adenosine kinase can result in augmentation of the local adenosine concentrations at foci of tissue injury, further enhancing cytoprotection. This effect is likely to be most pronounced at tissue sites where trauma results in increased adenosine production, thereby minimizing systemic toxicities.

Pharmacologic compounds directed towards adenosine kinase inhibition provide potentially effective new therapies for disorders benefited by the site- and event-specific potentiation of adenosine. Disorders where such compounds may be useful include ischemic conditions such as cerebral ischemia, myocardial ischemia, angina, coronary artery bypass graft surgery (CABG), percutaneous transluminal angioplasty (PTCA), stroke, other thrombotic and embolic conditions, and neurological disorders such as epilepsy, anxiety, schizophrenia, nociperception including pain perception, neuropathic pain, visceral pain, as well as inflammation, arthritis, immunosuppression, sepsis, diabetes and gastrointestinal disfunctions such as abnormal gastrointestinal motility.

A number of compounds have been reported to inhibit adenosine kinase. The most potent of these include 5'-amino-5'-deoxyadenosine (Miller, *et al.*, *J. Biol. Chem.* 1979,

254: 2339-2345), 5-iodotubercidin (Wotring and Townsend, *Cancer Res.* 1979, **39**: 3018-3023) and 5'-deoxy-5-iodotubercidin (Davies, *et al.*, *Biochem. Pharmacol.* 1984, **33**: 347-355).

Adenosine kinase is also responsible for the activation of many pharmacologically active nucleosides (Miller, *et al.*, *J. Biol. Chem.* 1979, **254**: 2339-2345), including tubercidin, formycin, ribavirin, pyrazofurin and 6-(methylmercapto)purine riboside. These purine nucleoside analogs represent an important group of antimetabolites which possess cytotoxic, anticancer and antiviral properties. They serve as substrates for adenosine kinase and are phosphorylated by the enzyme to generate the active form. The loss of adenosine kinase activity has been implicated as a mechanism of cellular resistance to the pharmacological effects of these nucleoside analogs (*e.g.* Bennett, *et al.*, *Mol. Pharmacol.*, 1966, **2**: 432-443; Caldwell, *et al.*, *Can. J. Biochem.*, 1967, **45**: 735-744; Suttle, *et al.*, *Europ. J. Cancer*, 1981, **17**: 43-51). Decreased cellular levels of adenosine kinase have also been associated with resistance to the toxic effects of 2'-deoxyadenosine (Hershfield and Kredich, *Proc. Natl. Acad. Sci. USA*, 1980, **77**: 4292-4296). The accumulation of deoxyadenosine triphosphate (dATP), derived from the phosphorylation of 2'-deoxyadenosine, has been suggested as a toxic mechanism in the immune defect associated with inheritable adenosine deaminase deficiency (Kredich and Hershfield, in *The Metabolic Basis of Inherited Diseases*, 1989 (Scriver, *et al.*, eds.), McGraw-Hill, New York, pp. 1045-1075).

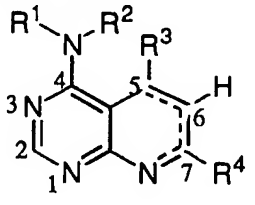
B.S. Hurlbert *et al.* (*J. Med. Chem.*, 11: 711-717 (**1968**)) disclose various 2,4-diaminopyrido[2,3-d]pyrimidine compounds having use as antibacterial agents. R. K. Robins *et al.* (*J. Amer. Chem. Soc.*, 80:3449-3457 (**1958**)) disclose methods for preparing a number of 2,4-dihydroxy-, 2,4-diamino-, 2-amino-4-hydroxy- and 2-mercapto-4-hydroxypyrido[2,3-d]pyrimidines having antifolic acid activity. R. Sharma *et al.*, (*Indian J. Chem.*, 31B: 719-720 (**1992**)) disclose 4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine and 4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine compounds having antibacterial activity. A. Gupta *et al.*, (*J. Indian Chem. Soc.*, 71: 635-636 (**1994**)) disclose 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine and 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine compounds having antibacterial activity. L. Prakash *et al.*, *Pharmazie*, 48: 221-222 (**1993**)) disclose 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine, 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine, 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine, and 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine compounds having antifungal activity. P. Victory *et al.*, *Tetrahedron*, 51: 10253-10258 (**1995**)) discloses the synthesis of 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine compounds from

acyclic precursors. Bridges *et al.*(PCT application WO 95/19774, published July 27, 1995) disclose various bicyclic heteroaromatic compounds as having utility for inhibiting tyrosine kinase of epidermal growth factors.

Summary Of The Invention

The present invention provides for 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds having utility as adenosine kinase inhibitors.

In one aspect, the present invention provides a method of inhibiting adenosine kinase by administering a compound of formula (I)



(I)

wherein

R^1 and R^2 are independently selected from H, loweralkyl, C_1-C_6alkoxyC_1-C_6alkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group, heteroarylalkyl or heterocycloalkyl wherein the heteroaryl and heterocyclic groups are linked directly or indirectly by a ring carbon;

R^4 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group heteroarylalkyl or heterocycloalkyl; and a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained.

In particular, the method of inhibiting adenosine kinase comprises exposing an adenosine kinase to an effective inhibiting amount of a compound of Formula I of the present invention. Where the adenosine kinase is located *in vivo*, the compound is administered to the organism.

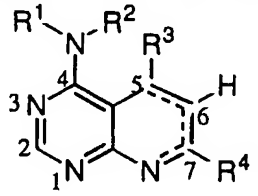
In still another aspect, the present invention provides a method of treating ischemia, neurological disorders, nociperception , inflammation, immunosuppression, gastrointestinal disfunctions, diabetes and sepsis in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound of Formula I of the present invention.

In a preferred aspect, the present invention provides a method of treating cerebral

ischemia, myocardial ischemia, angina, coronary artery bypass graft surgery, percutaneous transluminal angioplasty, stroke, thrombotic and embolic conditions, epilepsy, anxiety, schizophrenia, pain perception, neuropathic pain, visceral pain, arthritis, sepsis, diabetes and abnormal gastrointestinal motility in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound of Formula I of the present invention.

The present invention also contemplates the use of pharmaceutically acceptable salts and amides of compounds having Formula I.

In another aspect, the present invention provides a compound of formula (I)



(I)

wherein

R^1 and R^2 are independently selected from H, loweralkyl, C_1-C_6alkoxyC_1-C_6alkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group, heteroarylalkyl or heterocycloalkyl wherein the heteroaryl and heterocyclic groups are linked directly or indirectly by a ring carbon;

R^4 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group heteroarylalkyl or heterocycloalkyl; and a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

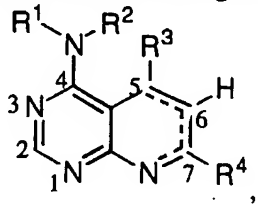
with the proviso that the compound may not be selected from the group consisting of:

(a) 4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
(b) 4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
(c) 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;
(d) 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;
(e) 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;
(f) 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;
(g) 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;
(h) 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine; and

(i) 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

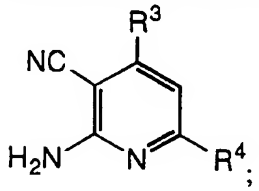
In another aspect, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula I above in combination with a pharmaceutically acceptable carrier.

In another aspect, the present invention provides a process for the preparation of adenosine kinase inhibiting compounds having the formula



, wherein R^1 and R^2 are hydrogen, the method comprising

(a) contacting a ketone having the formula R^4-CO-CH_3, wherein R^4 is as defined above, with an aldehyde having the formula R^3-CHO, wherein R^3 is as defined above and malononitrile in the presence of an ammonium salt under anhydrous conditions and isolating a first intermediate compound having the structure



;

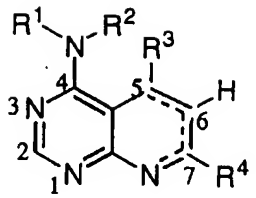
(b) contacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula I with double bonds between the 7 and 8 position and the 5 and 6 position and optionally reducing to form a partially saturated right side or a fully saturated right side to form a compound of formula I.

Detailed Description of the Invention

The present invention relates to 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds that are useful in inhibiting adenosine kinase, to pharmaceutical compositions containing such compounds, to a method of using such compounds for inhibiting adenosine kinase, and to novel 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds.

In one aspect, the present invention provides 5,7-disubstituted-4-aminopyrido[2,3-d]pyrimidine compounds that are adenosine kinase inhibitors. An adenosine kinase inhibitor of the present invention is a compound of the Formula I, shown above.

As summarized above, the present invention relates to a method of inhibiting adenosine kinase comprising administering a compound of formula I



(I)

wherein

R^1 and R^2 are independently selected from H, loweralkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to from a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 and R^4 are independently selected from the group consisting of:

C_1-C_6alkyl,

C_2-C_6alkenyl,

C_2-C_6alkynyl,

C_3-C_8cycloalkyl,

heteroarylC_0-C_6alkyl or substituted heteroarylC_0-C_6alkyl,

optionally substituted cycloalkyl,

arylC_0-C_6alkyl or substituted arylC_0-C_6alkyl,

heteroarylC_2-C_6alkenyl or substituted heteroarylC_2-C_6alkenyl,

arylC_2-C_6alkenyl or substituted arylC_2-C_6alkenyl,

heteroarylC_2-C_6alkynyl or substituted heteroarylC_2-C_6alkynyl,

arylC_2-C_6alkynyl or substituted arylC_2-C_6alkynyl wherein the 1-4 heteroaryl or aryl substituents are independently selected from

halogen, oxo, CO_2R^5, cyanoC_1-C_6alkyl, heteroarylC_0-C_6alkyl, heterocyclicC_0-C_6alkyl, C_1-C_6alkyloxy, C_1-C_6alkyloxyC_1-C_6alkyl, arylC_0-C_6alkyl, arylC_1-C_6alkyloxy, R^5R^6NC(O), cyano, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6alkyl, C_2-C_6alkenyldialkylmalonyl, CF_3, HO-, C_1-C_6alkyloxyC_1-C_6alkyloxy, C_1-C_6alkylSO_n wherein n is 1-2, C_1-C_6alkylthio, C_1-C_6alkylacryl, CF_3O, CF_3, C_1-C_4alkylenedioxy, C_1-C_6alkylacryl, R^5R^6N(CO)NR^5, N-formyl(heterocyclic), NO_2, $NR^5R^6C_0$-C_6alkyl, (R^5O)(R^6O)-P(O)- C_0-C_6alkyl,

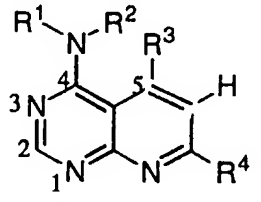
wherein R^5 and R^6 are independently selected from H, C_1-C_6alkyl, HC(O), C_1-C_6alkyloxyC_1-C_6alkyl, C_1-C_6alkyloxy, C_1-C_6alkylC(O), CF_3C(O), $NR^7R^8C_1$-C_6alkyl, phthalimidoC_1-C_6C(O), C_1-C_6alkylSO_n where n is 1-2, CNC_1-C_6alkyl, R^7R^8NC(O)NR^7-, heteroaryl, $NR^7R^8C_1$-C_6alkylC(O), C_1-C_6alkyloxycarbamidoC_1-C_6alkyl,

wherein R^7 and R^8 are independently selected from those variables identified for R^5 and R^6 or

R^5 and R^6 or R^7 and R^8 may join together with the nitrogen atom to which they are attached to form a 5-7 membered unsubstituted or substituted ring optionally containing 1-3 additional heteroatoms selected from O, N or S wherein the substituents are selected from C_1-C_6alkyl and

a dashed line --- indicates a double bond is optionally present.

The preferred compounds utilized in the above method of inhibiting adenosine kinase are selected from a compound of formula II



(II)

wherein R^1-R^8 and n are as defined above. The present invention also relates to compounds of formula II with R^1-R^8 and n as defined above with the proviso that the specific known compounds identified above for a compound of formula I are excluded.

In a preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula (II) above, wherein R^4 is aryl or heteroaryl and substituted versions thereof.

In a more preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula (II) above, wherein R^4 is aryl or heteroaryl and substituted versions thereof and R^3 is loweralkyl, aryl, arylalkyl or heteroaryl and substituted versions thereof wherein the substituents are as identified above.

In another preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula (I) above, wherein R^4 is selected from the group consisting of: phenyl; thiophene-2-yl; 3-methyl-2-oxobenzoxazolin-6-yl; 2-(dimethylamino)-5-pyrimidinyl; 2-(N-formyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methylamino)-5-pyrimidinyl; 2-(1-morpholinyl)-5-pyrimidinyl; 2-(1-pyrrolidinyl)-5-pyrimidinyl; 2-dimethylamino-5-pyrimidinyl; 2-furanyl; 2-oxobenzoxazolin-6-yl; 2-pyridyl; 3-(dimethylamino)phenyl; 3-amino-4-methoxyphenyl; 3-bromo-4-(dimethylamino)phenyl; 3-methoxyphenyl; 3-methyl-4-(N-acetyl-N-methylamino)phenyl; 3-methyl-4-(N-formyl-N-methylamino)phenyl; 3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl; 3-methyl-4-(N-methylamino)phenyl; 3-methyl-4-pyrrolidinylphenyl; 3-pyridyl; 3,4-dichlorophenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 4-(acetylamino)phenyl; 4-(dimethylamino)-3-fluorophenyl; 4-

(dimethylamino)phenyl; 4-(imidazol-1-yl)phenyl; 4-(methylthio)phenyl; 4-(morpholinyl)phenyl; 4-(N-(2-(dimethylamino)ethyl)amino)phenyl; 4-(N-(2-methoxyethyl)amino)phenyl; 4-(N-acetyl-N-methylamino)phenyl; 4-(N-ethyl-N-formylamino)phenyl; 4-(N-ethylamino)phenyl; 4-(N-formyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-isopropylamino)phenyl; 4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl; 4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl; 4-(N-methyl-N-(2-cyano)ethylamino)phenyl; 4-(N-methyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-methyl-N-(3-methoxy)propionylamino)phenyl; 4-(N-methyl-N-acetylamino)phenyl; 4-(N-methyl-N-formylamino)phenyl; 4-(N-methyl-N-trifluoroacetylamino)phenyl; 4-(N-morpholinyl)phenyl; 4-(thiophene-2-yl)phenyl; 4-(ureido)phenyl; 4-(2-(dimethylamino)acetylamino)phenyl; 4-(2-(2-methoxy)acetylamino)ethyl)amino)phenyl; 4-(2-methoxy)ethoxyphenyl; 4-(2-oxo-3-oxazolidinyl)phenyl; 4-(4-methoxy-2-butyl)phenyl; 4-(4-methylpiperidinyl)phenyl; 4-(5-pyrimidinyl)phenyl; 4-aminophenyl; 4-bromophenyl; 4-butoxyphenyl; 4-carboxamidophenyl; 4-chlorophenyl; 4-cyanophenyl; 4-diethylaminophenyl; 4-diethylmalonylallylphenyl); 4-dimethylaminophenyl; 4-ethoxyphenyl; 4-ethylphenyl; 4-fluorophenyl; 4-hydroxyphenyl; 4-imidazolylphenyl; 4-iodophenyl; 4-isopropylphenyl; 4-methoxyphenyl; 4-methylaminophenyl; 4-methylsulfonylphenyl; 4-morpholinylphenyl; 4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl; 4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl; 4-N-ethyl-N-(2-methoxyethyl)amino)phenyl; 4-N-formylpiperazinylphenyl; 4-nitrophenyl; 4-piperidinylphenyl; 4-(3-pyridyl)phenyl; 4-pyrrolidinylphenyl; 4-t-butylacrylphenyl; 5-(dimethylamino)thiophene-2-yl; 5-amino-2-pyridyl; 5-dimethylamino-2-pyrazinyl; 3-dimethylaminopyridazin-6-yl; 5-dimethylamino-2-pyridyl; 5-pyrimidinylphenyl; 6-(N-methyl-N-formylamino)-3-pyridinyl; 6-(N-methyl-N-methoxyethylamino)-3-pyridinyl; 6-(2-oxo-3-oxazolidinyl)-3-pyridinyl; 6-dimethylamino-3-pyridinyl; 6-imidazolyl-3-pyridinyl; 6-morpholinyl-3-pyridinyl; 6-pyrrolidinyl-3-pyridinyl; 6-(2-propyl)-3-pyridinyl; and (4-formylamino)phenyl.

In another preferred embodiment, an adenosine kinase inhibitor of the present invention is a compound of Formula (I) above, wherein R^3 is selected from the group consisting of: (thiophene-2-yl)methyl; (thiophene-3-yl)methyl; butyl; cycloheptyl; pentyl; thiophene-2-yl; 1-(3-bromophenyl)ethyl; 2-(N-phenylmethoxycarbonyl)aminophenyl; 2-(3-bromophenyl)ethyl; 2-(3-cyanophenyl)methyl; 2-(4-bromophenyl)ethyl; 2-(5-chloro-2-(thiophen-3-yl)phenyl; 2-bromophenyl; 2-furanyl; 2-methylpropyl; 2-phenylethyl; phenylmethyl; 2,3-dimethoxyphenyl; 2,3-methylenedioxyphenyl; 3-(furan-2-yl)phenyl; 3-(thiophen-2-yl)phenyl; 3-(2-pyridyl)phenyl; 3-(3-methoxybenzyl)phenyl; 2-(3-aminopropynyl)phenylmethyl; 3-benzyloxyphenyl; 3-bromo-4-fluorophenyl; 3-bromo-5-

iodophenyl; 3-bromo-5-methoxyphenyl; 3-bromophenyl; 3-bromophenylmethyl; 3-carboxamidophenyl; 3-chlorophenyl; 3-cyanophenyl; 3-diethylmalonylallylphenyl; 3-dimethylaminophenyl; 3-ethoxyphenyl; 3-fluoro-5-trifluoromethylphenyl; 3-fluorophenyl; 3-hydroxyphenyl; 3-iodophenyl; 3-methoxyethyoxyphenyl; 3-methoxyphenyl; 3-methylphenyl; 3-methylsulfonylphenyl; 3-methylthiophenyl; 3-t-butylacrylphenyl; 3-trifloromethyoxyphenyl; 3-trifluoromethylphenyl; 3-vinylpyridinylphenyl; 3,4-dichlorophenyl; 3,4-dimethoxyphenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 3,5-di(trifluoromethyl)phenyl; 3,5-dibromophenyl; 3,5-dichlorophenyl; 3,5-dimethoxyphenyl; 3,5-dimethylphenyl; 4-(2-propyl)phenyl; 4-(2-propyl)oxyphenyl; 4-benzyloxyphenyl; 4-bromophenyl; 4-bromothiophene-2-yl; 4-butoxyphenyl; 4-dimethylaminophenyl; 4-fluoro-3-trifluoromethylphenyl; 4-methoxyphenyl; 4-neopentylphenyl; 4-phenoxyphenyl; 5-bromothiophene-2-yl; 5-cyclohexyl; 5-cyclopropyl; 5-hexyl; 5-methyl; 5-phenyl; (2-bromo-5-chlorophenyl)methyl; (2-bromophenyl)methyl; and (5-chloro-2-(3-methoxyphenyl)phenyl)methyl.

Exemplary and preferred adenosine kinase inhibitor compounds of the invention utilized in the method recited herein include the compounds listed below wherein R^1 and R^2 in a compound of formula II are selected from H, the groups identified at the 5-position are included within R^3 and the groups identified at the 7-position are included within R^4, R^5-R^8 are as described in the specific compound:

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacrylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-phenylpyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifloromethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido [2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;
4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine:

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl))-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

and pharmaceutically acceptable salts and amides thereof. In addition, the and pharmaceutically acceptable salts and amides thereof. The partially saturated and fully saturated versions of the above compounds are also included within the scope of the method of inhibiting adenosine kinase in a patient in need of treatment thereof. The above compounds may be treated with hydrogen and a catalyst to form a compound of formula I

wherein the double bonds on the right side are absent or there is a double bond between the 5,6 carbons; the 6,7 carbons or the 7 carbon, 8 nitrogen.

Exemplary and preferred compounds of the invention, again with the variables R^1-R^8 as specifically shown below, include:

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacrylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-phenylpyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifloromethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;

4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl))-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2.3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3.2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

and pharmaceutically acceptable salts and amides thereof. In addition, the partially hydrogenated or fully hydrogenated versions wherein the 5,6 and/or the 7,8 double bonds are hydrogenated of the compounds identified above are also included within the scope of the invention. The preferred substitution pattern on the R^3 group when it is selected from, for example, a substituted aryl group, is having at least one substituent at the meta position. The preferred substitution pattern on the R^4 position when it is selected from, for example, a substituted heteroaryl group, is having at least one substituent at the para position. The present invention is therefore directed to compounds of formula I or II with the variables recited as above wherein, in the case of R^3 selected from substituted aryl or heteroaryl groups and R^4 selected from substituted aryl or heteroaryl groups, the substiuents on the R^3 group are meta and the substituents on the R^4 group are para. In addition, the present invention encompasses pro-drugs of the above compounds which may be active in their own right or are metabolized or converted to the non pro-drug form as exemplified above. The invention is not limited to synthetic versions of the claimed compounds and includes the compounds-per-se or pro-drugs or metabolites thereof regardless of how or where they are manufactured or made.

The term "acyl", as used herein, refers to a moiety attached by a carbonyl linkage, as for example, loweralkyl-carbonyl or aryl-carbonyl, wherein loweralkyl and aryl are as defined herein. Examples of acyl include, for example, acetyl, propionyl, hexanoyl, trifluoroacetyl, benzoyl, 4-methylbenzoyl, methoxyacetyl, pentanoyl, N-Bocglycylimidazoyl, N-phthalimidylglycyl and the like or others as specified herein.

The term "aryl" or "substituted aryl" as used herein, refers to a carbocyclic aromatic radical, including, for example, phenyl and 1- or 2-naphthyl, which may be unsubstituted or substituted respectively by independent replacement of one, two or three of the hydrogen atoms thereon with Cl, Br, F, I, cyano, carboxamido, hydroxy, loweralkoxy, loweralkyl, loweralkenyl, loweralkynyl, amino, loweralkylamino, di(loweralkylamino), N-loweralkyl-N-loweralkoxyamino, trifluoromethyl or methoxymethyl groups. In addition, the term "aryl" refers to a phenyl group substituted with one ureido, methylsulfonyl, pyrimidinyl, pyridinyl, pyridazinyl, morpholinyl, phenyl-loweralkoxy, phenyl-loweralkenyl or cycloalkyl-loweralkyl group. Examples of aryl radicals include, but are not limited to, 3-bromophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-methoxyphenyl, 3-(2-propyl)phenyl, 3,4-dimethoxyphenyl, 3-trifluromethylphenyl, 3-trifluoro-4-fluorophenyl, 4-(N-methyl-N-methoxyl)ethylaminophenyl, 4-dimethylaminophenyl, 3-fluoro-4-methylphenyl, 4-methylphenyl, 4-cyanophenyl, 4-propylmethyl, 3,5-dichlorophenyl, 3,4-methylenedioxyphenyl, 3-cyanopropylphenyl, 4-ureidophenyl, 3-methylsulfonylphenyl, 3-carboxamidopropylphenyl.

The term "arylalkyl" refers to a loweralkyl radical having appended thereto an aryl group, as defined above, as for example benzyl and phenylethyl.

The term "aryloxy" refers to a aryl radical which is appended to the molecule via an ether linkage (*i.e.*, through an oxygen atom), as for example phenoxy, naphthyloxy, 4-chlorophenoxy, 4-methylphenoxy, 3,5-dimethoxypehenoxy, and the like.

The term "cycloalkyl" refers to a cyclic saturated hydrocarbon radical having from 3 to 7 ring atoms. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl. Cycloalkyl is also described as C_3-C_8cycloalkyl.

The term "cycloalkyl-loweralkyl" refers to a loweralkyl radical as defined below substituted with a cycloalkyl group as defined above by replacement of one hydrogen atom. Examples of cycloalkyl-loweralkyl include cyclopropylmethyl, cyclobutylethyl, cyclopentylmethyl, cyclohexylmethyl and cycloheptylbutyl, and the like.

The term "heteroaryl" or "substituted heteroaryl" refers to a monocyclic aromatic radical having from five to seven ring atoms of which one ring atom is nitrogen, oxygen or sulfur; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon, the radical being joined to the rest of the molecule via any of the ring atoms. A heteroaryl group may be unsubstituted or

substituted by independent replacement of one, two or three of the hydrogen atoms thereon with Cl, Br, F, I, cyano, carboxamido, hydroxy, loweralkoxy, loweralkyl, loweralkenyl, loweralkynyl, amino, loweralkylamino, di(loweralkylamino), N-loweralkyl-N-loweralkoxyamino, trifluoromethyl or methoxymethyl groups. In addition, the term "heteroaryl " refers to a heteroaryl group substituted with one ureido, methylsulfonyl, pyrimidinyl, pyridinyl, pyridazinyl, morpholinyl, phenyl-loweralkoxy, phenyl-loweralkenyl or cycloalkyl-loweralkyl group. In addition a heteroaryl group may be substituted by replacement of any two adjacent hydrogen atoms with a grouping of atoms to form a fused benzene ring, e.g., benz derivatives such as indole, benzoxazole and the like. Examples of heteroaryl include pyridinyl, pyrazinyl, pyrimidinyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, thiadiazolyl, oxadiazolyl, furanyl, thiophenyl, 5-methylthiophene-2-yl, 5-nitrothiophene-2-yl, 5-methylfuranyl, benzofuranyl, benzothiophenyl, and the like and those additionally described herein.

The term "heterocyclic" refers to a saturated or unsaturated monocyclic ring system radical having from four to seven ring atoms of which one is nitrogen or oxygen; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remainder are carbon, the radical being joined to the rest of the molecule via any of the ring carbon atoms and being optionally substituted, either on a nitrogen or a carbon atom, by an additional radical selected from among aryl(loweralkyl), alkoxycarbonyl, loweralkyl, halo(loweralkyl), amino(loweralkyl), hydroxy-substituted loweralkyl, hydroxy, loweralkoxy, halogen, amino, loweralkylamino, and amino, (loweralkyl)amino or alkanoylamino of from one to eight carbon atoms in which the amino group may be further substituted with alkanoyl of from one to eight carbons, an alpha-amino acid or a polypeptide. Examples of heterocyclic include pyrrolidine, tetrahydrofuran, dihydropyrrole, isoxazolidine, oxazolidine, tetrahydropyridine, piperidine, piperazine, morpholine, thiomorpholine, aziridine and azetidine or those additionally described herein.

The term "heterocyclic-loweralkyl" refers to a loweralkyl radical as defined below substituted with a heterocyclic-group as defined above by replacement of one hydrogen atom. Examples of cycloalkyl-loweralkyl include pyrrolidinylmethyl, piperidinylethyl, and the like.

The term "loweralkyl", as used herein, refers to saturated, straight- or branched-chain hydrocarbon radicals containing from one to six carbon atoms including, which may be unsubstituted or substituted by independent replacement of one, two or three of the hydrogen atoms thereon with Cl, Br, F, I, cyano, carboxamido, hydroxy, loweralkoxy, amino, loweralkylamino, iminoloweralkylamino,di(loweralkylamino) or N-loweralkyl-N-loweralkoxyamino groups. Examples of loweralkyl include, but are not limited to, methyl, ethyl, propyl, isopropyl, *n*-butyl, *tert*-butyl, neopentyl, n-hexyl, hydroxyethyl,

methoxymethyl, trifluoromethyl, 3-cyanopropyl, 3-carboxamidopropyl, and the like. In certain cases, the group "C_1-C_6alkyl" is described and has a similar meaning as above for loweralkyl but is more specifically recited. Likewise, the term "C_0-C_6alkyl" indicates the carbon atoms which may be present in the alkyl chain including zero. These terms are also provided adjacent to aryl or heteroaryl or other generic group and represent or have the same meaning as, for example, "arylalkyl" or "heteroarylalkyl".

The term "loweralkenyl", as used herein, refers to mono-unsaturated straight- or branched-chain hydrocarbon radicals containing from two to six carbon atoms including, but not limited to, vinyl, propenyl, *n*-butenyl, *i*-butenyl, *n*-pentenyl, and n-hexenyl. These variables are also recited as, for example, C_2-C_6alkenyl.

The term "loweralkoxy" refers to a loweralkyl radical which is appended to the molecule via an ether linkage (*i.e.*, through an oxygen atom), as for example methoxy, ethoxy, propoxy, 2-propoxy, 2-methyl-2-propoxy, *tert*-butoxy, pentyloxy, hexyloxy, isomeric forms thereof and the like. This term is also described as C_1-C_6alkyloxy.

The term "loweralkynyl", as used herein, refers to straight- or branched-chain hydrocarbon radicals possessing a single triple bond and containing from two to six carbon atoms including, but not limited to, ethynyl, propynyl, *n*-butynyl, *n*-pentynyl, and n-hexynyl. This term is also described as C_2-C_6alkynyl.

The term "mammal" has its ordinary meaning and includes human beings.

In a further aspect of the present invention pharmaceutical compositions are disclosed which comprise a compound of the present invention in combination with a pharmaceutically acceptable carrier.

The present invention includes one or more compounds, as set forth above, formulated into compositions together with one or more non-toxic physiologically tolerable or acceptable diluents, carriers, adjuvants or vehicles that are collectively referred to herein as diluents, for parenteral injection, for oral administration in solid or liquid form, for rectal or topical administration, or the like. As is well known in the art, a compound of the present invention can exist in a variety of forms including pharmaceutically-acceptable salts, amides and the like.

Compositions may be prepared that will deliver the correct amount of a compound or compounds of the invention. The following dosages are thought to provide the optimal therapy: <u>iv infusions</u>: 0.1- 250 nmol/kg/minute, preferably from 1-50 nmol/kg/minute; <u>oral</u>: 0.01-250 μMol/kg/day, preferably from about 0.1-50 μMol/kg/day; these oral molar dosage ranges correspond to 0.005-125 mg/kg/day, preferably 0.05-25 mg/kg/day. For treatment of acute disorders the preferred route of administration is intravenous; the preferred method of treating chronic disorders is orally by means of a tablet or sustained release formulation.

"Pharmaceutically-acceptable amide" refers to the pharmaceutically-acceptable, nontoxic amides of the compounds of the present invention which include amides formed with suitable organic acids or with amino acids, including short peptides consisting of from 1-to-6 amino acids joined by amide linkages which may be branched or linear, wherein the amino acids are selected independently from naturally-occurring amino acids, such as for example, glycine, alanine, leucine, valine, phenylalanine, proline, methionine, tryptophan, asparagine, aspartic acid, glutamic acid, glutamine, serine, threonine, lysine, arginine, tyrosine, histidine, ornithine, and the like.

"Pharmaceutically-acceptable salts" refers to the pharmaceutically-acceptable, nontoxic, inorganic or organic acid addition salts of the compounds of the present invention, as described in greater detail below.

The compounds of the present invention can be used in the form of pharmaceutically-acceptable salts derived from inorganic or organic acids. These salts include, but are not limited to, the following: acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, flavianate, fumarate, glucoheptonate, glycerophosphate, hemisulfate, heptonate, hexonoate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxy-ethanesulfonate, lactate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmoate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, and undecanoate.

Appropriate cationic salts are also readily prepared by conventional procedures such as treating an acid of Formula I with an appropriate amount of base, such as an alkali or alkaline earth metal hydroxide, *e.g.*, sodium, potassium, lithium, calcium, or magnesium, or an organic base such as an amine, *e.g.*, dibenzylethylenediamine, cyclohexylamine, dicyclohexylamine, triethylamine, piperidine, pyrrolidine, benzylamine, and the like, or a quaternary ammonium hydroxide such as tetramethylammonium hydroxide and the like. Also, the basic nitrogen-containing groups can be quaternized with such agents as loweralkyl halides, such as methyl, ethyl, propyl, and butyl chlorides, bromides, and iodides; dialkyl sulfates; long chain halides such as decyl, lauryl, myristyl, and stearyl chlorides, bromides and iodides; arylalkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

The salts of the present invention can be synthesized from the compounds of Formula I which contain a basic or acidic moiety by conventional methods, such as by reacting the free base or acid with stoichiometric amounts or with an excess of the desired salt forming inorganic acid or base in a suitable solvent or various combinations of solvents.

Further included within the scope of the present invention are pharmaceutical compositions comprising one or more of the compounds of formula (I) prepared and formulated in combination with one or more non-toxic pharmaceutically acceptable carriers compositions, in the manner described below.

Compositions suitable for parenteral injection may comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions and sterile powders for reconstitution into sterile injectable solutions or dispersions. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (propylene glycol, polyethylene glycol, glycerol, and the like), suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl oleate. Proper fluidity may be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preserving, wetting, emulsifying, and dispersing agents. Prevention of the action of microorganisms may be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include isotonic agents, for example, sugars, sodium chloride and the like. Prolonged absorption of the injectable pharmaceutical form may be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

If desired, and for more effective distribution, the compounds may be incorporated into slow-release or targeted-delivery systems, such as polymer matrices, liposomes, and microspheres. They may be sterilized, for example, by filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions, which may be dissolved in sterile water, or some other sterile injectable medium immediately before use.

Solid dosage forms for oral administration may include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is admixed with at least one inert customary excipient (or carrier), such as sodium citrate or dicalcium phosphate, and additionally (a) fillers or extenders, as for example, starches, lactose, sucrose, glucose, mannitol and silicic acid; (b) binders, as for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose and acacia; (c) humectants, as for example, glycerol; (d) disintegrating agents, as for example, agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain complex silicates and sodium carbonate; (e) solution retarders, as for example paraffin; (f) absorption accelerators, as for example, quaternary ammonium compounds; (g) wetting agents, as for example, cetyl alcohol and glycerol monostearate; (h) adsorbents, as for example, kaolin and bentonite; and

(i) lubricants, as for example, talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate or mixtures thereof. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents.

Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules, using such excipients as lactose or milk sugar, as well as high molecular weight polyethylene glycols, and the like.

Solid dosage forms such as tablets, dragees, capsules, pills and granules may be prepared with coatings and shells, such as enteric coatings and others well known in this art. They may contain pacifying agents, and may also be of such composition that they release the active compound or compounds in a certain part of the intestinal tract in a delayed manner. Examples of embedding compositions which may be used are polymeric substances and waxes.

The active compounds may also be in micro-encapsulated form, if appropriate, with one or more of the above-mentioned excipients.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art, such as water or other solvents, solubilizing agents and emulsifiers, as for example, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethylformamide, oils, in particular, cottonseed oil, groundnut oil, corn germ oil, olive oil, castor oil and sesame oil, glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan or mixtures of these substances, and the like.

Besides such inert diluents, these liquid dosage forms may also include adjuvants, such as wetting agents, emulsifying and suspending agents, sweetening, flavoring and perfuming agents.

Suspensions, in addition to the active compounds, may contain suspending agents, as for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, or mixtures of these substances, and the like.

Compositions for rectal or vaginal administrations are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating excipients or carriers such as cocoa butter, polyethylene glycol or a suppository wax, which are solid at ordinary temperatures but liquid at body temperature and therefore, melt in the rectum or vaginal cavity and release the active component.

Dosage forms for topical or transdermal administration of a compound of this invention further include ointments, pastes, creams, lotions, gels, powders, solutions,

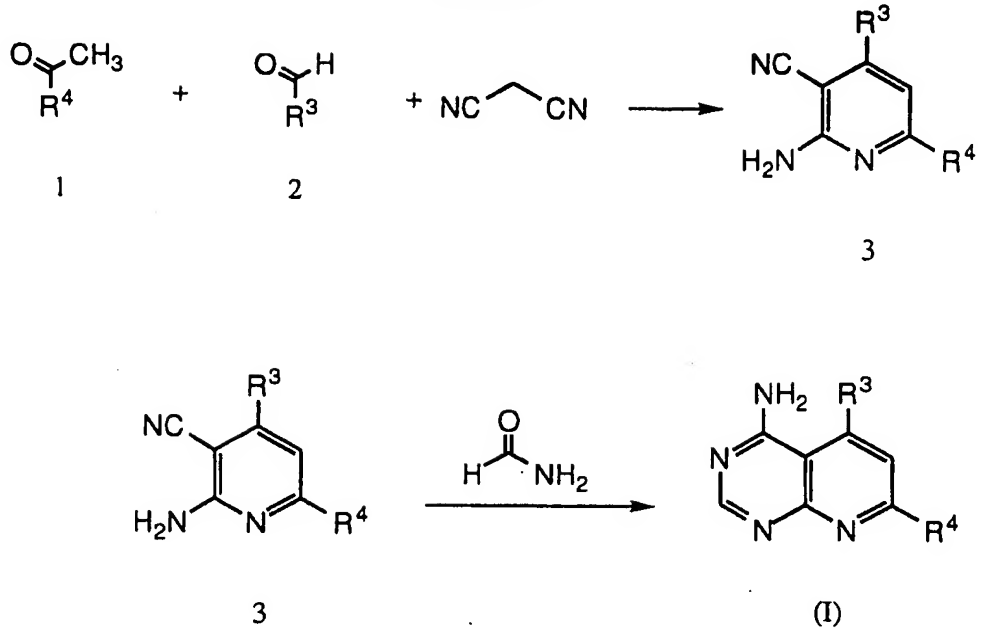
sprays, inhalants or transdermal patches. Transdermal administration via a transdermal patch is a particularly effective and preferred dosage form of the present invention. The active component is admixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservative, buffers or propellants as may be required. It is known that some agents may require special handling in the preparation of transdermal patch formulations. For example, compounds that are volatile in nature may require admixture with special formulating agents or with special packaging materials to assure proper dosage delivery. In addition, compounds which are very rapidly absorbed through the skin may require formulation with absorption-retarding agents or barriers. Ophthalmic formulations, eye ointments, powders and solutions are also contemplated as being within the scope of this invention.

The present compounds may also be administered in the form of liposomes. As is known in the art, liposomes are generally derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multi-lamellar hydrated liquid crystals that are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolizable lipid capable of forming liposomes may be used. The present compositions in liposome form may contain, in addition to the compounds of the present invention, stabilizers, preservatives, excipients, and the like. The preferred lipids are the phospholipids and the phosphatidyl cholines (lecithins), both natural and synthetic. Methods to form liposomes are known in the art. See, for example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N. Y., (1976), p 33 *et seq.*

Synthetic Methods

The compounds and processes of the present invention will be better understood in connection with the following synthetic schemes which illustrate the methods by which the compounds of the invention may be prepared. The R groups are as defined above unless otherwise noted below.

Scheme 1



The compounds of the present invention may be synthesized by methods illustrated in Schemes 1 and 2. In accordance with Scheme 1, the 5,7-disubstituted compounds wherein R^4 and R^3 are aryl, heteroaryl, or a heterocyclic group may be prepared by a modification of a method of Kambe *et al.*, *Synthesis*, **1980,** 366-368. An appropriately substituted acetophenone (1, the "R^4 Reagent"), wherein R^4 is aryl, heteroaryl, or a heterocyclic group, an appropriately substituted aldehyde (2, the "R^3 Reagent"), R^3 is aryl, heteroaryl, or a heterocyclic group, and malononitrile are heated in the presence of ammonium acetate, or another suitable ammonium salt, such as for example, ammonium propionate, ammonium iodide, or the like, in an aprotic solvent to produce compound (3). The water of the reaction may removed by use of a Dean Stark apparatus or by another suitable means, such as 4 Å molecular sieves. Suitable aprotic solvents include benzene, toluene, methylene chloride, DMF, THF, dioxane, and the like. The reaction may be performed at from about 40 °C to about 200 °C, and preferably at the reflux temperature of the solvent, for from about 1 hour to about 24 hours, preferably about 4 hours to 8 hours. The product (3) is preferably purified by chromatography after isolation from the reaction mixture. The above reaction may also proceed by contacting the aldehyde (2) with malononitrile and isolating the resulting dicyano R^3substituted alkene which is then reacted with the ketone (1) to form, upon addition of ammonium and cyclization, compound (3). Aliphatic aldehydes do not work effectively by this route. The ketone (1) may, however, include R^4 as alkyl groups.

The acetophenone starting materials (1) may be obtained commercially, or prepared easily by Friedel-Craft acylation of a suitable aromatic substrate, for example. The appropriate aldehyde starting materials (2) also may be obtained commercially, or may be prepared easily, for example by reductions of esters or acids with DIBAL or another suitable hydride reducing agent, or oxidation of alcohols under Swern conditions, for example.

Compound (3) is then treated with excess formamide by heating at reflux. The formation of product is monitored by TLC, and when the reaction is complete (after about 1 to about 8 hours) the reaction mixture is cooled to room temperature. The 5,7-disubstituted pyrido[2,3-d]pyrimidine product (I) is then removed by filtration and purified by column chromatography. This compound may then be partially or fully reduced by catalytic hydrogenation to the partially saturated or fully saturated version(s) (on the right side of the molecule) of the compounds shown in Scheme 1 or of Formula I. Stereoisomers produced during these reduction steps are included within the scope of the invention. The present invention also contemplates reductions which produce single bonds between the 5,6 and 7,8 positions and a double bond between the 6,7 carbons. The stereoisomers may be isolated and purified by conventional means.

In accordance with Scheme 2 are prepared compounds of Formula (I) wherein R^4 is preferrably an aryl, heteroaryl or heterocyclic group, and R^3 is loweralkyl, loweralkenyl, loweralkynyl, or an arylalkyl group. In addition, R^4 may be selected from those additional groups listed in R^3.

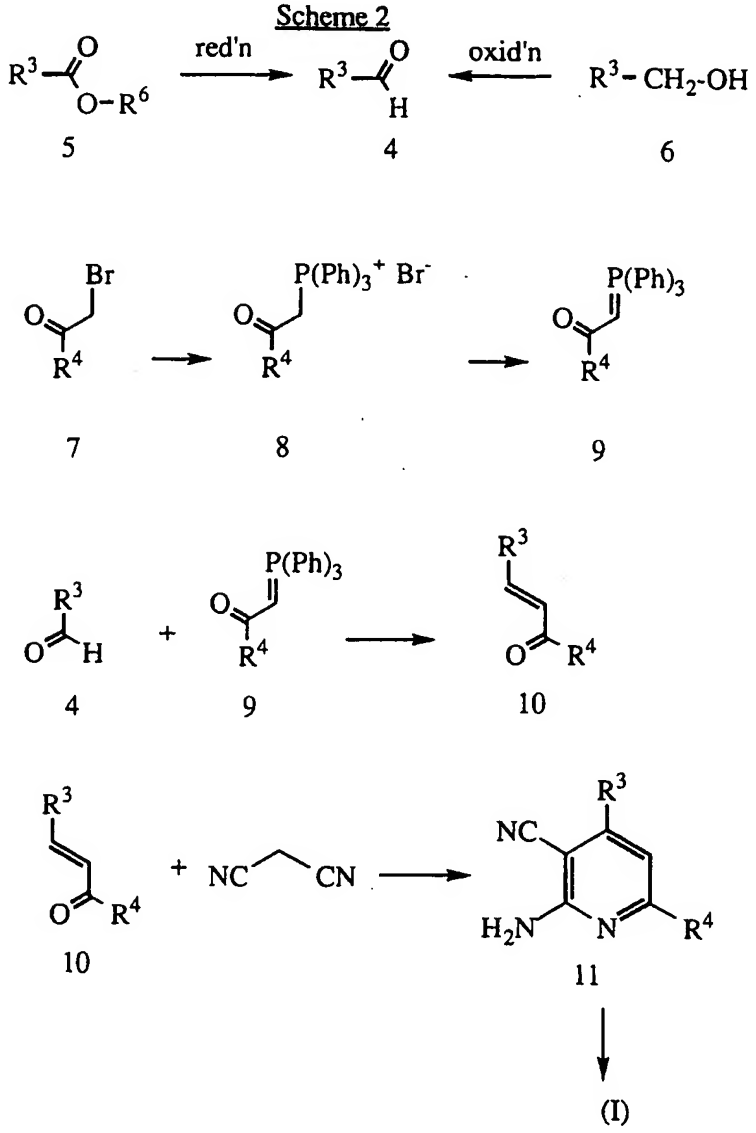
Compound (4, the "R^3 Reagent") may be obtained commercially or prepared from the precursor ester (5) or alcohol (5) by suitable reactions. Compound (5) may be reduced with a suitable reducing agent, such as for example, diisobutylaluminum hydride or another similar alkylaluminum hydride, under conditions well known to the art. Compound (6) may be oxidized to the aldehyde (4) Swern oxidation conditions, or other reactions known to those skilled in the art. The desired compound (4) is freshly prepared before its use in the reaction described below.

Compound (9), the "R^4 Reagent")) may be prepared from the precursor alpha-bromo ketone (7) by a two-step procedure. Compound (7) is treated with triphenylphosphine in the presence of a base, such as for example, triethyl amine, to give compound (8). Compound (8) is then treated with an alkali metal base, such as NaOH or the like, to give compound (9). The procedure is normally accomplished by vigorous mixing of a solution of (8) in an organic solvent with an aqueous solution of base.

Compounds (4) and (9) are mixed and the mixture is held at ambient temperature until the reaction is complete (monitoring by TLC), and the product (10) is purified by chromatography. A mixture of the cis and trans isomers is obtained and taken to the next step without further separation. Compound (10) is condensed with malononitrile by

heating in the presence of ammonium acetate as defined for Scheme 1 above to produce compound (11).

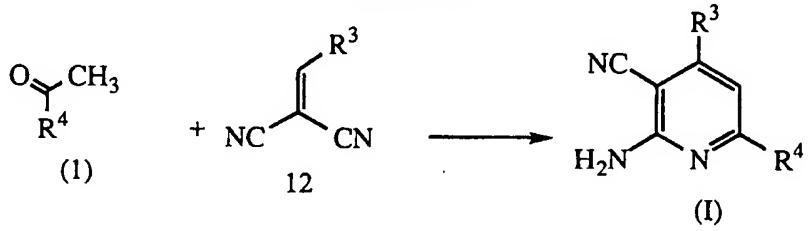
Scheme 2



Compound (11) is then treated with excess formamide by heating at reflux. The formation of product is monitored by TLC, and when the reaction is complete (routinely, after about 1 to about 8 hours) the reaction mixture is cooled to room temperature. The 5,7-disubstituted pyrido[2,3-d]pyrimidine product (I) is then removed by filtration and purified by column chromatography. In an alternate procedure, compound (11) is treated by heating with formamidine acetate in ethoxyethanol, followed by purification by flash chromatography. In another alternate procedure, compound (11) and ammonium sulfate are

heated at reflux in triethyl orthoformate for about 1 to about 8 hours, but preferably about 2 hours. The reaction mixture is cooled and added to a mixture of ammonia in ethanol. The mixture is stirred for about 12 to 24 hours at 25 °C, then at reflux for from one to 4 hours, and the solvent is removed in vacuo. The residue is purified by trituration with chloroform/ethyl acetate, and the product may be converted to a hydrochloride salt by suspension in 3M HCl, followed by lyophilization.

Scheme 3



Scheme 3 illustrates an alternate method for preparing the compounds (I) of the invention. Compounds (1), prepared as described above, are reacted with a dicyanoalkene compound (12) by heating with a suitable ammonium salt, such as for example, ammonium acetate, ammonium propionate, ammonium iodide, or the like, at reflux in an alcoholic or aprotic solvent to give the compound (I). Suitable solvents for the reaction may be easily determined by those skilled in the art, without undue trial and error, and may include, for example, ethanol, propanol, isopropanol, t-butanol, n-butanol, 1,2-dichloroethane, benzene, chloroform, carbon tetrachloride, toluene, dioxane, dimethoxyethane, and the like. A preferred solvent is 1,2-dichloroethane. The dicyano compounds (12) may be prepared from the precursor aldehyde (4) by treatment with malononitrile in 1:1 H_2O:EtOH in the presence of a catalytic amount of glycine according to the method of Bastus (*Tetrahedron Lett.*, 1963: 955), or alternately MgO in dichloromethane or a similar aprotic solvent (cf. Broekhuis, et al., Recl. J. R. Neth. Chem. Soc., 99: 6-12 (1980); Moison, *et al.* Tetrahedron (1987), 43:537-542).

To prepare compounds of formula (I) wherein R^1 and R^2 are not both hydrogen atoms, it is possible to prepared the desired derivative from the compound of Formula (I) wherein R^1 and R^2 are both hydrogen atoms. When R^1 or R^2 is loweralkyl this may be accomplished by reaction of the free amino group with the appropriate alkylating reagent, such as an alkyl halide, an alkyl mesylate or an alkyl tosylate, for example, in the presence of a base such as triethylamine or potassium carbonate in a suitable solvent, such as for example, methylene chloride or THF. When R^1 or R^2 is arylalkyl this may be accomplished by reaction of the free amino group with the appropriate arylalkyl halide, an alkyl mesylate

or an alkyl tosylate, for example, in the presence of a base such as triethylamine or potassium carbonate in a suitable solvent, such as for example, methylene chloride or THF. When R^1 or R^2 is acyl this may be accomplished by reaction of the free amino group with the appropriate acid anhydride, acyl chloride or activated acyl group, in the presence of a base such as triethylamine or potassium carbonate in a suitable solvent, such as for example, methylene chloride or THF. When R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form a 5-to-7 membered ring optionally containing an additional oxygen or nitrogen atom, the compound may be prepared by reacting a precursor compound having a halogen atom in place of the amino group at the 4-position with a 5-7 membered ring compound optionally containing an additional oxygen or nitrogen atom. Examples of such compounds include, but are not limited to, morpholine, piperidine, pyrrolidine, piperazine, thiomorpholine, and the like. Also, this alternate procedure may be used to prepare alkyl substituted amino compounds, for example by reacting the chloro compound with a mono- or disubstituted amine, such as for example, diethylamine, allyl amine, dibutylamine. This reaction takes place readily in a solvent such as methylene chloride, for example, in the presence of a tertiary amine. The precursor compound having a halogen atom in place of the amino group at the 4-position may be prepared by substitution of triethyl orthoformate for the formamide followed by chlorination of the ring by treatment with phosphorous oxychloride or thionyl chloride in the presence of DMF in Scheme 1 wherein compound (3) is converted to compound (I).

Method of Inhibiting Kinase

In yet another aspect of the present invention a process of inhibiting adenosine kinase is disclosed. In accordance with that process, an adenosine kinase enzyme is exposed to an effective inhibiting amount of an adenosine kinase inhibitor compound of the present invention. Preferred such compounds for use in the process are the same as set forth above. Means for determining an effective inhibiting amount are well known in the art.

The adenosine kinase to be inhibited can be located *in vitro, in situ or in vivo*. Where the adenosine kinase is located *in vitro*, adenosine kinase is contacted with the inhibitor compound, typically by adding the compound to an aqueous solution containing the enzyme, radiolabeled substrate adenosine, magnesium chloride and ATP. The enzyme can exist in intact cells or in isolated subcellular fractions containing the enzyme. The enzyme is then maintained in the presence of the inhibitor for a period of time and under suitable physiological conditions. Means for determining maintenance times are well known in the art and depend inter alia on the concentrations of enzyme and the physiological conditions. Suitable physiological conditions are those necessary to maintain adenosine

kinase viability and include temperature, acidity, tonicity and the like. Inhibition of adenosine kinase can be performed, by example, according to standard procedures well known in the art (Yamada, *et al.*, *Comp. Biochem. Physiol.* 1982, **71B**: 367-372).

Where the adenosine kinase is located *in situ* or *in vivo*, is typically administered to a fluid perfusing the tissue containing the enzyme. That fluid can be a naturally occuring fluid such as blood or plasma or an artificial fluid such as saline, Ringer's solution and the like. A method of inhibiting adenosine kinase *in vivo* is particularly useful in mammals such as humans. Administering an inhibitor compound is typically accomplished by the parenteral (*e.g.*, intravenous injection or oral) administration of the compound. The amount administered is an effective inhibiting or therapeutic amount.

By a "therapeutically-effective amount" of the compound of the invention is meant a sufficient amount of the compound to treat adenosine kinase related disorders or those conditions or diseases which are ameliorated or modified by local inhibition of the enzyme which results in an increase in the concentration of adenosine. It will be understood, however, that the total daily usage of the compounds and compositions of the present invention is to be decided by the attending physician within the scope of sound medical judgment. The specific therapeutically-effective dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; activity of the specific compound employed; the specific composition employed; the age, body weight, general health, gender and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with specific compound employed; and the like factors well known in the medical arts and well within the capabilities of attending physicians.

Compounds of the present invention inhibit adenosine kinase activity *in vitro* and *in vivo*. *In vitro* adenosine kinase activity can be measured using any of the standard procedures well known in the art. By way of example, cells containing adenosine kinase, such as IMR-32 human neuroblastoma cells, are cultured in the presence and absence of an inhibitor. Inhibition is measured as the ability to inhibit phosphorylation of endogenous or externally applied ^{14}C-adenosine by these cells. The cells can be intact or broken. The specificity of adenosine kinase inhibitory activity is determined by studying the effects of inhibitors on adenosine A1 and A2α receptor binding, adenosine deaminase activity and adenosine transport.

Compounds of the present invention are effective in inhibiting adenosine kinase activity *in vivo*. Numerous animal models for studying adenosine kinase activity and the affects of inhibiting such activity are well known in the art. By way of example, adenosine kinase inhibitors have been reported to protect rodents (*e.g.*, mice and rats) from seizures

induced by the subcutaneous administration of pentylenetetrazol (PTZ). Typically the rodents are injected with various doses of a given inhibitor followed at various times by the subcutaneous administration of from about 10 to about 500 milligrams per kilogram of PTZ. The injected animals are then observed for the onset of seizures.

The compounds of the invention were tested *in vivo* in the hot plate test of analgesia in mammals such as mice. For example, the compounds of examples 6, 79, 104, 130, 133, 134, 137, 205, 246 and 256 in the procedure described directly below were tested thirty minutes after pretreatment with the drugs (30 μmol/kg i.p.) for latency to 10th jump (in seconds). The longer the number of seconds, the more effective the drug at masking the pain felt from the hot plate. Compound 6 resulted in 152 seconds relative to the vehicle alone of 72.8±10.5 seconds (average±standard deviation); compound 79 resulted in 143 seconds; compound 104 resulted in 180 seconds; compound 130 resulted in 158 seconds; compound 133 resulted in 131 seconds; compound 134 resulted in 137 seconds; compound 137 resulted in 159 seconds; compound 205 resulted in 158 seconds, compound 246 resulted in 160 seconds and compound 256 resulted in 143 seconds. Compounds of the invention are therefore potent pain relievers as demonstrated in this animal model.

Mouse Hot Plate Assay

Male CF1 mice (Charles River) of approximately 25-30 g body weight are pretreated with 10 ml/kg of the test compounds, i.p. or p.o, in groups of 8 animals per dose. At the end of the pretreatment period, the mice are placed in an Omnitech Electronics Automated 16 Animal Hot Plate Analgesia Monitor (Columbus, OH; Model AHP16AN) in individual, 9.8 x 7.2 x 15.3 cm (l x w x h) plastic enclosures on top of a copper plate warmed to 55°C. Infared sensors located near the top of each enclosure record beam crossings that occur as the mice jump off of the heated surface. Latency times for each jump are automatically recorded, and latency to both the first and tenth jumps are used for data analysis. Mice that do not reach the criteria of 10 jumps by 180 seconds are immediately removed from the hotplate to avoid tissue damage, and they are assigned the maximum value of 180 seconds as their latency to tenth jump.

Numerous other animal models of adenosine kinase activity have been described [See, *e.g.*, Davies,, *et al., Biochem. Pharmacol.*, **33**:347-355 (1984); Keil, *et al., Eur. J. Pharmacol.*, **271**:37-46 (1994); *Murray, et al., Drug Development Res.*, **28**:410-415 (1993)].

Compounds of the present invention were also tested *in vitro* . The results of some representative studies are shown below in Tables 1 below. The Examples provided before the claims are all adenosine kinase inhibitors. The data indicate that the compounds inhibit adenosine kinase and are useful as adenosine kinase inhibitors. The compounds of the

invention including compounds of formula I and II with the variables recited herein are also useful as screening tools or as comparative indicators of adenosine kinase inhibition activity relative to unknown inhibitors or potential inhibitors.

Table 1

Inhibition of Adenosine Kinase by Representative Compounds of the Invention

Compound of Example No.	IC_{50} (nM)
6	200
15	7
44	50
53	3
56	35
57	1
64	8
79	5
81	3
100	2
104	2
130	1
133	2
137	5
147	150
150	150
170	1
175	300
177	25
201	3
205	3
208	4
246	5
247	3
256	1
270	20
272	>100
274	2
283	8
288	0.3
290	1
291	0.6
292	10
303	1
304	1
306	0.3
308	2
309	0.1
315	0.3
319	1

327	1
330	5
333	2
336	8
337	4
338	4.5
347	3

Method of Treating Cerebral Ischemia, Epilepsy, Nociperception (Nociception) (Pain), Inflammation including conditions such as Septic Shock due to Sepsis Infection

In yet another aspect of the present invention a method of treating cerebral ischemia, epilepsy, nociperception or nociception, inflammation including conditions such as septic shock due to sepsis infection in a human or lower mammal is disclosed, comprising administering to the mammal a therapeutically effective amount of a compound of formula I with R^1-R^8 as defined herein. The preferred compounds are those of formula II with the R variables as defined previously. In particular, the present invention relates to a method of treating the above disorders comprising administering a compound of formula II wherein R^3 is a substituted aryl or heteroaryl moiety wherein the substituent (preferrably halogen) is at the meta position relative to the ring attachment and R^4 is a substituted heteroaryl or aryl moiety wherein the substituent is at the para position relative to the ring attachment. The most preferred use is in the treatment of pain.

Alterations in cellular adenosine kinase activity have been observed in certain disorders. Adenosine kinase activity was found to be decreased, relative to normal liver, in a variety of rat hepatomas: activity of the enzyme giving a negative correlation with tumor growth rate (Jackson, *et al., Br. J. Cancer*, 1978, **37**: 701-713). Adenosine kinase activity was also diminished in regenerating liver after partial hepatectomy in experimental animals (Jackson, *et al., Br. J. Cancer*, 1978, **37**: 701-713). Erythrocyte Adenosine kinase activity was found to be diminished in patients with gout (Nishizawa, *et al., Clin. Chim. Acta* 1976, **67**: 15-20). Lymphocyte adenosine kinase activity was decreased in patients infected with the human immunodeficiency virus (HIV) exhibiting symptoms of AIDS, and increased in asymptomatic HIV-seropositive and HIV-seronegative high-risk subjects, compared to normal healthy controls (Renouf, *et al., Clin. Chem.* 1989, **35**: 1478-1481). It has been suggested that measurement of adenosine kinase activity may prove useful in monitoring the clinical progress of patients with HIV infection (Renouf, *et al., Clin. Chem.* 1989, **35**: 1478-1481). Sepsis infection may lead to a systemic inflammatory syndrome (SIRS), characterized by an increase in cytokine production, neutrophil accumulation, hemodynamic effects, and tissue damage or death. The ability of adenosine kinase inhibitor to elevate adenosine levels in tissues has been demonstrated to ameliorate syndrome symptoms, due to

the known anti-inflammatory effects of adenosine. (Firestein, et al., *J. of Immunology*, 1994: 5853-5859). The ability of adenosine kinase inhibitors to elevate adenosine levels is expected to alleviate pain states, since it has been demonstrated that administration of adenosine or its analogs results in antinociception or antinociperception. (Swaynok, *et al.*, *Neuroscience*, 1989, **32**:557-569).

The following Examples illustrate preferred embodiments of the present invention and are not limiting of the specification and claims in any way.

Example 1

4-amino-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine

A sample of 4-(4-bromophenyl)-3-cyano-6-(4-(dimethylamino)phenyl)pyridine-2-amine (1 g), was suspended in formamide (20 mL), and the reaction was heated to reflux. After about 3 hours, the reaction was complete as monitored by TLC, and the reaction mixture was cooled to room temperature. The product was allowed to precipitate, then recovered by filtration and washed with water. Additional product was recovered from the filtrate. The product was purified by column chromatography eluting with 10% $MeOH/CH_2Cl_2$ to give the pure title compound. IR (KBr) 3503, 3398, 1731, 1658, 1510, 1467, 1278cm^{-1}; MS *m/z* 421 $(M+H)^+$.

The 4-(4-bromophenyl)-3-cyano-6-(4-(dimethylamino)phenyl)pyridine-2-amine compound was prepared as follows:

The reagents, 4-bromoacetophenone (10 mmol, the "R^4 reagent"), 4-dimethylaminobenzaldehyde (10 mmol, the "R^3 reagent"), malononitrile (10 mmol) and ammonium acetate (1.4 g) were added to 25 mL of benzene. The reaction mixture was heated to reflux in a vessel fitted with a Dean-Stork apparatus. After 3.5 hours, the mixture was cooled, and the solvent was removed. The residue was purified by flash chromatography, eluting with methylene chloride, with optional addition of 5% ethyl acetate to the eluant. MS *m/z* 394 $(M+H)^+$.

Examples 2-156

Following the procedures of Example 1, except substituting the appropriate reagents for R^4 and R^3 as indicated in Table 2 below, compounds of Examples 2-156 were prepared.

Table 2
Examples 2-156

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
2	4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylamino-phenyl)-ethanone	4-dimethylamino-benzaldehyde	IR (KBr) 3440, 1615, 1760, 1210cm^{-1}; MS *m/z* 385 $(M+H)^+$.
3	4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylamino-phenyl)-ethanone	4-methoxybenzaldehyde	IR (KBr) 3330, 1600, 1640, 1780, 1200cm^{-1}; MS *m/z* 372$(M+H)^+$.
4	4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-dimethylamino-benzaldehyde	IR (KBr) 3660, 1600, 1620, 1510, 1360, 1240 cm^{-1}; MS *m/z* 372 $(M+H)^+$.
5	4-amino-5-(4-isopropylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-isopropyl-benzaldehyde	IR (KBr) 3430, 3360, 1580, 1540 cm^{-1}; MS *m/z* 371 $(M+H)^+$.
6	4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-neopentyl-benzaldehyde	IR (KBr) 3480, 2960, 1580, 1510, 1240 cm^{-1}; MS *m/z* 399 $(M+H)^+$.
7	4-amino-5-(4-butoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-butoxybenzaldehyde	IR (KBr) 3480,1600, 1580, 1510, 1240, 1180 cm^{-1}; MS *m/z* 401 $(M+H)^+$.
8	4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;	1-(4-bromophenyl)-ethanone	4-methoxybenzaldehyde	IR (KBr) 3660, 1600, 1680, 1520, 1240cm^{-1}; MS *m/z* 407$(M+H)^+$.
9	4-amino-5-(4-isopropoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-isopropoxy-benzaldehyde	IR (KBr) 3480, 2940, 1600, 1580, 1504 cm^{-1}; MS *m/z* 386 $(M+H)^+$.
10	4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-formylpiperazinylphenyl)-ethanone	4-butoxy-benzaldehyde	IR (KBr) 3480, 2940, 1660, 1600, 1580, 1510 cm^{-1}; MS *m/z* 483 $(M+H)^+$.
11	4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-benzyloxy-benzaldehyde	IR (KBr) 3480, 3040, 1600, 1580, 1560 cm^{-1}; MS *m/z* 435 $(M+H)^+$.

12	4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-phenoxy-benzaldehyde	IR (KBr) 3456, 3053, 1580, 1558, 1247 cm^{-1}; MS *m/z* 421 $(M+H)^+$.
13	4-amino-5-(4-isopropylphenyl)-7-(4-diethylmalonylallylphenyl) pyrido[2,3-d]pyrimidine;	1-(4-(3-(diethylmalonyl) allyl) phenyl)-ethanone	4-isopropyl-benzaldehyde	IR (KBr) 3480, 2980, 1735, 1580, 1555 cm^{-1}; MS *m/z* 539 $(M+H)^+$.
14	4-amino-5-(4-isopropylphenyl)-7-(4-t-butylacrylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-t-butylacrylphenyl)-ethanone	4-isopropyl-benzaldehyde	IR (KBr) 3471, 2957, 1708, 1584, 1556, 1149 cm^{-1}; MS *m/z* 467 $(M+H)^+$.
15	4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1560, 1360, 1200 cm^{-1}; MS *m/z* 421 $(M+H)^+$.
16	4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,4-dimethoxy-benzaldehyde	IR (KBr) 3450, 1610, 1580, 1560, 1510 cm^{-1}; MS *m/z* 402 $(M+H)^+$.
17	4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(3-formylphenyl)acrylic acid t-butyl ester	IR (KBr) 3480, 3400, 1700, 1610, 1580, 1560 cm^{-1}; MS *m/z* 468 $(M+H)^+$.
18	4-amino-5-(3-methoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-methoxy-benzaldehyde	IR (KBr) 3475, 1610, 1580, 1560, 1200 cm^{-1}; MS *m/z* 372 $(M+H)^+$.
19	4-amino-5-(3,5-dimethoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3419, 1637, 1600, 1572, 1371, 1202 cm^{-1}; MS *m/z* 402 $(M+H)^+$.
20	4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	2-[2-(3-formylphenyl)vinyl]malonic acid diethyl ester	IR (KBr) 3480, 1720, 1610, 1580, 1558, 1524,1360 cm^{-1}; MS *m/z* 540 $(M+H)^+$.
21	4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-vinylpyridinyl-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1560, 1513, 1360 cm^{-1}; MS *m/z* 385 $(M+H)^+$.
22	4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-trifluoromethyl-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1560, 1360, 1200 cm^{-1}; MS *m/z* 410 $(M+H)^+$.

23	4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-amido-benzaldehyde	IR (KBr) 3480, 1610, 1580, 1380, 1200 cm^{-1}; MS *m/z* 446 $(M+H)^+$.
24	4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-cyano-benzaldehyde	IR (KBr) 3460, 3400, 2210, 1610, 1580, 1554, 1360 cm^{-1}; MS *m/z* 367 $(M+H)^+$.
25	4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-benzyloxy-benzaldehyde	IR (KBr) 3470, 1640, 1580, 1550, 1515, 1357, 1250 cm^{-1}; MS *m/z* 448 $(M+H)^+$.
26	4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	3-methoxy-benzaldehyde	IR (KBr) 3470, 1640, 1580, 1550, 1515, 1357, 1250, 1240, 1180 cm^{-1}; MS *m/z* 359 $(M+H)^+$.
27	4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-butoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1610, 1580, 1560, 1515, 1355, 1255, 1240, 1180 cm^{-1}; MS *m/z* 449 $(M+H)^+$.
28	4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(2-pyridyl)-benzaldehyde	IR (microscope) 3476, 1609, 1580, 1560, 1358 cm^{-1}; MS *m/z* 419 $(M+H)^+$.
29	4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-methyl-benzaldehyde	IR (microscope) 3400, 1640,1600, 1580, 1540cm^{-1}; MS *m/z* 356 $(M+H)^+$.
30	4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3400, 1600, 1580, 1540 cm^{-1}; MS *m/z* 376 $(M+H)^+$.
31	4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-fluoro-benzaldehyde	IR (microscope) 3480, 1640, 1580, 1560cm^{-1}; MS *m/z* 360 $(M+H)^+$.
32	4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3485, 1607, 1575, 1550, 1515, 1350, 1255, 1240, 1180, 1030 cm^{-1}; MS *m/z* 407 $(M+H)^+$.

33	4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;	1-(4-bromophenyl)-ethanone	3-methoxy-benzaldehyde	IR (microscope) 3450, 1640, 1573, 1555, 1496, 1350, 1260 cm^{-1}; MS *m/z* 407 $(M+H)^+$.
34	4-amino-5-(3-bromophenyl)-7-phenyl pyrido [2,3-d]pyrimidine;	1-phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1640, 1580, 1560, 1480, 1350, 700 cm^{-1}; MS *m/z* 377 $(M+H)^+$.
35	4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-ethylphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3480, 1645, 1580 (broad), 1490, 1380 cm^{-1}; MS *m/z* 405 $(M+H)^+$.
36	4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;	1-(4-bromophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1610, 1575, 1540, 1350 cm^{-1}; MS *m/z* 455 $(M+H)^+$.
37	4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;	1-(4-cyanophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3480, 2230, 1618, 1580, 1555, 1545, 1350 cm^{-1}; MS *m/z* 402 $(M+H)^+$.
38	4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-hydroxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3481, 3060 (broad), 1645, 1580, 1560, 1544, 1360, 1240 1155 cm^{-1}; MS *m/z* 393 $(M+H)^+$.
39	4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-iodo-benzaldehyde	IR (microscope) 3500, 3040, 1640, 1600, 1580, 1560 cm^{-1}; MS *m/z* 468 $(M+H)^+$.
40	4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-ethoxy-benzaldehyde	IR (microscope) 3460, 3250, 1640, 1600, 1580, 1560 cm^{-1}; MS *m/z* 386 $(M+H)^+$.
41	4-amino-5-(3-trifloromethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-trifluoromethoxy-benzaldehyde	IR (microscope) 3480, 1710, 1610, 1580, 1560, 1540 cm^{-1}; MS *m/z* 426 $(M+H)^+$.
42	4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,5-dichloro-benzaldehyde	IR (microscope) 3500, 3040, 1640, 1600, 1580, 1560 cm^{-1}; MS *m/z* 411 $(M+H)^+$.

43	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (microscope) 3440, 3015, 1633, 1607, 1583 cm^{-1}; MS *m/z* 438 $(M+H)^+$.
44	4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-hydroxy-benzaldehyde	IR (microscope) 3450, 1640, 1610, 1580,1560 cm^{-1}; MS *m/z* 358 $(M+H)^+$.
45	4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3483, 1607, 1578, 1561, 1518, 1355, 1228 1120 cm^{-1}; MS *m/z* 462 $(M+H)^+$.
46	4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-piperidinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3486, 1606, 1561, 1540, 1519, 1353, 1231, 1199, 1128 cm^{-1}; MS *m/z* 460 $(M+H)^+$.
47	4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(imidazol-1-yl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3481, 1580, 1555, 1525, 1482, 1352, 1303, 1053 cm^{-1}; MS *m/z* 443 $(M+H)^+$.
48	4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-chlorophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3470, 1635, 1580, 1560, 1500, 1350, 1090 cm^{-1}; MS *m/z* 411 $(M+H)^+$.
49	4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-isopropylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1610, 1579, 1560, 1550, 1483, 1357 cm^{-1}; MS *m/z* 419 $(M+H)^+$.
50	4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-trifluorophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3481, 3289, 1616, 1579, 1547, 1324, 1312, 1122, 1070 cm^{-1}; MS *m/z* 445 $(M+H)^+$.
51	4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-diethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3481, 1607, 1578, 1561, 1533, 1353, 1200, 1155 cm^{-1}; MS *m/z* 448 $(M+H)^+$.
52	4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3,4,5-trimethoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3485, 1579, 1548, 1507, 1340, 1129 cm^{-1}; MS *m/z* 467 $(M+H)^+$.

53	4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(3-methoxybenzyl)-benzaldehyde	IR (KBr) 3425, 1613, 1580, 1558, 1537 cm^{-1}; MS *m/z* 478 $(M+H)^+$.
54	4-amino-5-(3-methoxyethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-methoxyethoxy-benzaldehyde	IR (KBr) 3469, 1610, 1580, 1560, 1357 cm^{-1}; MS *m/z* 416 $(M+H)^+$.
55	4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,4-methylenedioxy-benzaldehyde	IR (KBr) 3466, 16245, 1579, 1560 cm^{-1}; MS *m/z* 386 $(M+H)^+$.
56	4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-ethoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1607, 1579, 1560, 1517, 1360, 1238, 1180 cm^{-1}; MS *m/z* 421 $(M+H)^+$.
57	4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;	1-phenyl-ethanone	3-bromo-benzaldehyde	IR (KBr) 3470, 1579, 1560, 1547, 1429, 1361 cm^{-1}; MS *m/z* 383 $(M+H)^+$.
58	4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-fluorophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3476, 1600, 1580, 1555, 1515, 1350, 1230 cm^{-1}; MS *m/z* 395 $(M+H)^+$.
59	4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-dimethylamino-benzaldehyde	IR (KBr) 3436, 1601, 1580, 1563, 1534, 1200 cm^{-1}; MS *m/z* 385 $(M+H)^+$.
60	4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	benzaldehyde	IR (KBr) 3400, 1600, 1580, 1560, 1530, 1200 cm^{-1}; MS *m/z* 342 $(M+H)^+$.
61	4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3,4,5-trimethoxy-benzaldehyde	IR (KBr) 33460, 1607, 1578, 1127cm^{-1}; MS *m/z* 432 $(M+H)^+$.
62	4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;	1-(4-nitrophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3485, 1618, 1580, 1550, 1520, 1340, 860 cm^{-1}; MS *m/z* 422 $(M+H)^+$.

63	4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1610, 1575, 1570, 1540, 1350, 1000 cm^{-1}; MS *m/z* 503 $(M+H)^+$.
64	4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3,4-methylenedioxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3485, 1607, 1575, 1545, 1500, 1440, 1350, 1255, 1038 cm^{-1}; MS *m/z* 421 $(M+H)^+$.
65	4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	thiophene-2-carboxaldehyde	IR (KBr) 3480, 1607, 1580, 1560, 1226 cm^{-1}; MS *m/z* 390 $(M+H)^+$.
66	4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido [2,3-d]pyrimidine;	1-(thiophen-2-yl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3450, 1640, 1600, 1580, 1560 cm^{-1}; MS *m/z* 365 $(M+H)^+$.
67	4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;	1-(4-carboxamidophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3481, 1674, 1611, 1577, 1558, 1352 cm^{-1}; MS *m/z* 420 $(M+H)^+$.
68	4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)ethoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-(2-methoxy)ethoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1607, 1580, 1560, 1515, 1357, 1260, 1235, 1180, 1113 cm^{-1}; MS *m/z* 451 $(M+H)^+$.
69	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3450, 1608, 1580, 1555, 1541, 1230, 1210, 1160 cm^{-1}; MS *m/z* 444 $(M+H)^+$.
70	4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;	1-(thiophene-2-yl)-ethanone	3-trifluoromethyl-benzaldehyde	IR (KBr) 3486, 1620, 1580, 1560, 1325, 1123cm^{-1}; MS *m/z* 373 $(M+H)^+$.
71	4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-aminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3450, 1632, 1605, 1580, 1365 cm^{-1}; MS *m/z* 393 $(M+H)^+$.
72	4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;	1-(thiophene-2-yl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (KBr) 3480, 1640, 1580, 1560, 1500cm^{-1}; MS *m/z* 401 $(M+H)^+$.
73	4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido [2,3-d]pyrimidine;	1-(2-furanyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (KBr) 3460, 1600, 1580, 1560, 1500cm^{-1}; MS *m/z* 385 $(M+H)^+$.

74	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3460, 1604, 1575, 1556, 1541, 1207, 1160 cm^{-1}; MS *m/z* 485 $(M+H)^+$.
75	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-imidazolylphenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3459, 1604, 1580, 1556, 1524, 1484, 1304, 1159, 1056 cm^{-1}; MS *m/z* 425 $(M+H)^+$.
76	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(thiophene-2-yl)phenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3457, 1602, 1579, 1557, 1207, 1159 cm^{-1}; MS *m/z* 441 $(M+H)^+$.
77	4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(3-pyridyl)phenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (KBr) 3452, 1604, 1578, 1558, 1287, 1206, 1159 cm^{-1}; MS *m/z* 436 $(M+H)^+$.
78	4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl) pyrido[2,3-d]pyrimidine;	1-(4-(4-methylpiperidinyl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1607, 1577, 1558, 1540, 1356, 1232 cm^{-1}; MS *m/z* 475 $(M+H)^+$.
79	4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-pyrrolidinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1608, 1577, 1560, 1533, 1353, 1196 cm^{-1}; MS *m/z* 446 $(M+H)^+$.
80	4-amino-5-(4-bromothiophen-2-yl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3327, 1604, 1578, 1548, 1521, 1367, 1350, 1202, 820 cm^{-1}; MS *m/z* 426 $(M+H)^+$.
81	4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3460, 1606, 1578, 1558, 1541, 1517, 1232, 824 cm^{-1}; MS *m/z* 468 $(M+H)^+$.
82	4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromophenyl-benzaldehyde	IR (microscope) 3340, 1603, 1580, 1540 cm^{-1}; MS *m/z* 490 $(M+H)^+$.
83	4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	5-bromothiophene-2-yl-benzaldehyde	IR (KBr) 3460, 1606, 1580, 1558, 1541, 1517, 1233 cm^{-1}; MS *m/z* 468 $(M+H)^+$.

84	4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	4-bromo-benzaldehyde	IR (microscope) 3480, 3320, 1603, 1580, 1540, 820 cm^{-1}; MS *m/z* 420 $(M+H)^+$.
85	4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(acetylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3480 1600, 1580, 1520cm^{-1}; MS *m/z* 434 $(M+H)^+$.
86	4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3300, 1606, 1600, 1580, 1560 cm^{-1}; MS *m/z* 421 $(M+H)^+$.
87	4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(5-pyrimidinylphenyl)-ethanone	3,5-dimethoxy-benzaldehyde	IR (microscope) 3458, 1602, 1579, 1558, 1460, 1414, 1364, 1196, 1058 cm^{-1}; MS *m/z* 437 $(M+H)^+$.
88	4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3410, 1605, 1570, 1525, 1503 cm^{-1}; MS *m/z* 514 $(M+H)^+$.
89	4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-pyrrolidinylphenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3470, 1609, 1577, 1555, 1520, 1409, 1386, 1350, 1196, 821 cm^{-1}; MS *m/z* 452 $(M+H)^+$.
90	4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;	1-(thiophene-2-yl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3308, 1606, 1578, 1543, 1526, 1427, 1359 cm^{-1}; MS *m/z* 389 $(M+H)^+$.
91	4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;	1-(5-(dimethylamino)thiophene-2-yl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3490, 1581, 1556, 1501, 1481, 1407, 1373, 1072 cm^{-1}; MS *m/z* 426 $(M+H)^+$.
92	4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3-bromo-5-iodo-benzaldehyde	IR (KBr) 3493, 1608, 1562, 1533, 1364, 1350, 1200 cm^{-1}; MS *m/z* 546 $(M+H)^+$.
93	4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3,5-di(trifluoromethyl-benzaldehyde	IR (KBr) 3484, 1607, 1580, 1554, 1386, 1280 cm^{-1}; MS *m/z* 478 $(M+H)^+$.

94	4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3,5-di(trifluoromethyl-benzaldehyde	IR (KBr) 3500, 1643, 1602, 1578, 1554, 1280 cm^{-1}; MS *m/z* 520 $(M+H)^+$.
95	4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3,5-dibromo-benzaldehyde	IR (KBr) 3440, 1608, 1570, 1559, 1536 cm^{-1}; MS *m/z* 475 $(M+H)^+$.
96	4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-morpholinylphenyl)-ethanone	3,5-dibromo-benzaldehyde	IR (KBr) 3480, 1607, 1560, 1540, 1225 cm^{-1}; MS *m/z* 540 $(M+H)^+$.
97	4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(4-methylpiperidinyl)phenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (KBr) 3460, 1608, 1576, 1557, 1540, 1513, 1384, 1353, 1240, 823 cm^{-1}; MS *m/z* 481 $(M+H)^+$.
98	4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3,5-dibromo-benzaldehyde	IR (KBr) 3486, 1608, 1570, 1559, 1536, 1360, 1350, 1200, 823 cm^{-1}; MS *m/z* 498 $(M+H)^+$.
99	4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1601, 1579, 1548, 1483, 1357 cm^{-1}; MS *m/z* 420 $(M+H)^+$.
100	4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylsulfonylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1600, 1580, 1550, 1490 cm^{-1}; MS *m/z* 455 $(M+H)^+$.
101	4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3-methoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1605, 1578, 1550, 1492, 1346, 1263 cm^{-1}; MS *m/z* 407 $(M+H)^+$.
102	4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(methylthio)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3485, 1607, 1578, 1566, 1538, 1350, 1094, 795 cm^{-1}; MS *m/z* 423 $(M+H)^+$.
103	4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;	1-(3,4-dichlorophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3482, 1634, 1576, 1545, 1488, 1342 cm^{-1}; MS *m/z* 445 $(M+H)^+$.

104	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-formylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1672, 1639, 1603, 1579, 1547, 841 cm^{-1}; MS *m/z* 434 $(M+H)^+$.
105	4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylaminophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3488, 1637, 1607, 1587, 1360 cm^{-1}; MS *m/z* 480 $(M+H)^+$.
106	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylsulfonylphenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (KBr) 3489, 1578, 1560, 1496, 1311, 1151, 775 cm^{-1}; MS *m/z* 473 $(M+H)^+$.
107	4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(3-amino-4-methoxyphenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3431, 1629, 1606, 1583, 1274 cm^{-1}; MS *m/z* 422 $(M+H)^+$.
108	4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-bromo-4-(dimethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3470, 1638, 1570, 1560, 1538, 1480, 1345 cm^{-1}; MS *m/z* 498 $(M+H)^+$.
109	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-bromo-4-(dimethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3438, 1640, 1605, 1580, 1555, 1368 cm^{-1}; MS *m/z* 434 $(M+H)^+$.
110	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-trifluoroacetylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3443, 1699, 1635, 1606, 1201 cm^{-1}; MS *m/z* 502 $(M+H)^+$.
111	4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;	1-(4-(dimethylamino)-3-fluorophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3438, 1638, 1592, 1365 cm^{-1}; MS *m/z* 438 $(M+H)^+$.
112	4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-ethyl-N-formylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3477, 1672, 1604, 1580, 1562, 1353 cm^{-1}; MS *m/z* 448 $(M+H)^+$.
113	4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-acetylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3434, 1667, 1635, 1600, 1200 cm^{-1}; MS *m/z* 532 $(M+H)^+$.

114	4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-acetyl-N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3443, 1667, 1635, 1600, 1200 cm^{-1}; MS *m/z* 532 $(M+H)^+$.
115	4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-ethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3441, 1633, 1603, 1572, 1368 cm^{-1}; MS *m/z* 420 $(M+H)^+$.
116	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(-(N-methyl-N-(2-methoxyethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3439, 1636, 1601, 1529, 1361 cm^{-1}; MS *m/z* 464 $(M+H)^+$.
117	4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(-(N-isopropylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3430, 1632, 1600, 1578, 1530, 1357 cm^{-1}; MS *m/z* 434 $(M+H)^+$.
118	4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3488, 1657, 1604, 1579,1552, 1118 cm^{-1}; MS *m/z* 506 $(M+H)^+$.
119	4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3201, 1679, 1617, 1597,1576, 1539, 1177, 1117 cm^{-1}; MS *m/z* 521 $(M+H)^+$.
120	4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1681, 1579, 1351, cm^{-1}; MS *m/z* 491 $(M+H)^+$.
121	4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3431, 1634, 1601, 1573, 1359 cm^{-1}; MS *m/z* 463 $(M+H)^+$.
122	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 2220, 1660, 1604, 1580,1560, 1352 cm^{-1}; MS *m/z* 459 $(M+H)^+$.
123	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1663, 1604, 1578,1559, 1352 1114 cm^{-1}; MS *m/z* 478 $(M+H)^+$.

124	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-formyl-N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3486, 1677, 1607, 1579, 1549, 1351 cm^{-1}; MS *m/z* 448 $(M+H)^+$.
125	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3433, 1635, 1605, 1585, 1359 cm^{-1}; MS *m/z* 420 $(M+H)^+$.
126	4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(4-methoxy-2-butyl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3473, 3063, 1710, 1671, 1582,1564, 1352 cm^{-1}; MS *m/z* 593 $(M+H)^+$.
127	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3443, 1638, 1606, 1582, 1359cm^{-1}; MS *m/z* 463 $(M+H)^+$.
128	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3484, 1701, 1610, 1579,1559, 1221, 1205, 1151 cm^{-1}; MS *m/z* 516 $(M+H)^+$.
129	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;	1-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1663, 1607, 1574,1547, 1354 cm^{-1}; MS *m/z* 462 $(M+H)^+$.
130	4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-dimethylamino-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3428, 1652, 1635, 1606, 1585, 1365 cm^{-1}; MS *m/z* 421 $(M+H)^+$.
131	4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methylsulfonylphenyl)-ethanone	3-cyano-benzaldehyde	IR (KBr) 3479, 1638, 1576,1559, 1303, 1147 cm^{-1}; MS *m/z* 402 $(M+H)^+$.
132	4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-formylamino)-phenyl)-ethanone	3-cyanobenzaldehyde	IR (KBr) 3418, 2230, 1688, 1674, 1584, 1554, 1114 cm^{-1}; MS *m/z* 381 $(M+H)^+$.
133	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(N-methyl-N-formylamino)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3474, 1676, 1577, 1561, 1353, 1130cm^{-1}; MS *m/z* 435 $(M+H)^+$.

134	4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-morpholinyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3487, 3396, 1601, 1580, 1558, 1234cm^{-1}; MS *m/z* 463 $(M+H)^+$.
135	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3476, 3307, 1702, 1683, 1605, 1560, 1116cm^{-1}; MS *m/z* 465 $(M+H)^+$.
136	4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-pyrrolidinyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3487, 3396, 1601, 1580, 1558, 1234 cm^{-1}; MS *m/z* 447 $(M+H)^+$.
137	4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(dimethylamino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3442 1640, 1604, 1577, 1536, 1408, 1367, 1348 cm^{-1}; MS *m/z* 422 $(M+H)^+$.
138	4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3439, 1640, 1606, 1587, 1556, 1537, 1374, 1347 cm^{-1}; MS *m/z* 466 $(M+H)^+$.
139	4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3472, 1687, 1583, 1565, 1459, 1353, 1142, 988 cm^{-1}; MS *m/z* 436 $(M+H)^+$.
140	4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-(N-methylamino)5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3483, 1605, 1550, 1346 cm^{-1}; MS *m/z* 408 $(M+H)^+$.
141	4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-pyrrolidinyl-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3468, 1600, 1581, 1552, 1527, 1482, 1330 cm^{-1}; MS *m/z* 448 $(M+H)^+$.
142	4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-morpholinyl-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) ? cm^{-1}; MS *m/z* 463 $(M+H)^+$.

143	4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3473, 1762, 1583, 1571, 1562, 1491, 1477, 1402, 1348, 1217 cm^{-1}; MS *m/z* 463 $(M+H)^+$.
144	4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;	1-(2-pyridyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3427, 3017, 1601, 783 cm^{-1}; MS *m/z* 351/353 $(M+H)^+$.
145	4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;	1-(3-pyridyl)-ethanone	3-bromo-benzaldehyde	IR (microscope) 3434, 3042, 1634, 1372 cm^{-1}; MS *m/z* 351/353 $(M+H)^+$.
146	4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(thiophen-2-yl)-benzaldehyde	IR (microscope) 3482, 2922, 1578, 1356 cm^{-1}; MS *m/z* 420/422 $(M+H)^+$.
147	4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(furan-2-yl)-benzaldehyde	IR (microscope) 3479, 3104, 1559, 1356 cm^{-1}; MS *m/z* 420/422 $(M+H)^+$.
148	4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	3-(3-methoxyphenyl)-benzaldehyde	IR (microscope) 3477, 2924, 1579, 1356 cm^{-1}; MS *m/z* 420/422 $(M+H)^+$.
149	4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;	1-(4-dimethylaminophenyl)-ethanone	benzaldehyde	IR (microscope) 3477, 3298, 1580, 1355 cm^{-1}; MS *m/z* 315 $(M+H)^+$.
150	4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(morpholinyl)phenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3480, 3056, 1579, 1356 cm^{-1}; MS *m/z* 391 $(M+H)^+$.
151	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(morpholinyl)phenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (microscope) 3491, 3044, 1560, 1230 cm^{-1}; MS *m/z* 453 $(M+H)^+$.
152	4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3478, 3280, 1539, 1350 cm^{-1}; MS *m/z* 432 $(M+H)^+$.
153	4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(thiophen-2-yl)phenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3484, 3055, 1560, 1354 cm^{-1}; MS *m/z* 459 $(M+H)^+$.
154	4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(5-pyrimidinyl)phenyl)-ethanone	3-chloro-benzaldehyde	IR (microscope) 3477, 3040, 1578, 1351 cm^{-1}; MS *m/z* 459 $(M+H)^+$.

155	4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;	1-(4-iodophenyl)-ethanone	3-bromo-4-fluoro-benzaldehyde	IR (microscope) 3444, 3048, 1607, 1356 cm^{-1}; MS *m/z* 494/496 $(M+H)^+$.
156	4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;	1-(4-methoxyphenyl)-ethanone	4-bromothiophene-2-carboxaldehyde	IR (microscope) 3460, 3300, 2900-3100, 1700, 1580, 1510 cm-1; MS *m/z* 413 $(M+H)^+$.

Example 157

4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine hydrochloride

A mixture of 3-cyano-4-(3-bromophenyl)methyl-6-(4-(dimethyl)aminophenyl)pyridine-2-amine (1.58 g) and ammonium sulfate (40 mg) in triethyl orthoformate was heated at reflux for 2 hours. The reaction mixture was cooled and added to a mixture of 8 g of ammonia in 150 mL of ethanol. After 16 hours at 25 °C, the reaction was heated at reflux for two hours, and the solvent was removed *in vacuo*. The residue was purified by chromatography, then converted to the hydrochloride salt by treatment with ether/HCl, followed by drying to give the title compound.

The 3-cyano-4-(3-bromophenyl)methyl-6-(4-(dimethyl)aminophenyl)pyridine-2-amine was prepared by a four-step procedure as follows:

step 157a: preparation of 3-bromophenylacetaldehyde (the "R^3 reagent")

To a solution of ethyl 3-bromophenylacetate (10.2 g, US patent 2,624,731 (**1950**)) in 230 mL of dichloromethane was added 42 mL of 1M Dibal-H in toluene at -78 °C with stirring. After 40 minutes at -78 °C, 10 mL of methanol was added, and the reaction allowed to warm to room temperature and partitioned between 50 mL of dichloromethane and 1200 mL of saturated aqueous potassium sodium tartrate. The organic layer was dried over sodium sulfate and the aldehyde used immediately in the next step without purification.

step 157b: preparation of α-(triphenylphosphonium)-4-(dimethylamino)phenylethan-1-one chloride

Following the procedure of Fukui *et al.* (*J. Org. Chem.* 33: 3594-3507 (**1968**)), α-bromo-(4-dimethylaminophenyl)ethan-1-one (the "R^4 reagent", CAS #37904-72-6; Chem. Abst. (1956), 864) was treated with triphenylphosphine in triethylamine and acetonitrile. The α-bromo-(4-dimethylaminophenyl)ethan-1-one was prepared by bromination with bromine in hydrobromic acid according to the method of Suzuki et al (J. Pharm. Soc. Japan,

(1955), 75:54. Removal of solvent and recrystallization from methanol/ethyl acetate/toluene gave the title product as a white powder.

step 157c: preparation of 1-(4-(dimethylamino)phenyl)-4-(3-bromophenyl)-but-2-en-1-one

20 g of α-(triphenylphosphonium)-4-(dimethylamino)phenylethan-1-one chloride (from step b) was partitioned between dichloromethane and 50 mL of 2N NaOH. The organic phase was dried over sodium sulfate and concentrated *in vacuo*. The residue was mixed with 3-bromophenylacetaldehyde (from step a) for 24 hours at 25 °C. The mixture was purified by chromatography to give 8.35 g (61%) of a cis/trans mixture of the title compound. The cis/trans mixture was taken to the next step without separation of the isomers.

step 157d: preparation of 3-cyano-4-(3-bromophenyl)methyl-6-(4-(dimethyl)aminophenyl)pyridine-2-amine

A mixture of 1-(4-(dimethylamino)phenyl)-4-(3-bromophenyl)-but-2-en-1-one chloride (3.85 g, from step c), ammonium acetate (2.6 g) and malononitrile (739 mg) in 3 mL of dimethoxyethane and 22 mL of ethanol was heated at 115 °C for 5 hours, then cooled and worked up by partitioning between dichloromethane and water. The residue obtained on concentration of the organic phase was purified by flash chromatography to give the title compound.

Examples 158-174

Following the procedures of Example 157, except substituting the appropriate reagents for the R^4 and R^3 reagents of Example 157 as indicated in Table 3 below, compounds of Examples 158-174 were prepared. The treatment with aqueous HCl was omitted, and the free bases were obtained except as indicated.

In Examples 167-174, the formamide or formamidine acetate (added periodically until the reaction was complete) treatment was replaced by treatment with triethyl orthoformate at reflux in the presence of a catalytic amount of ammonium sulfate, followed by cooling to 25 °C and addition of excess ammonia in ethanol. After 24 hours, the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichlorobenzene at 120-180 °C for 1-8 hours. The reaction mixture was cooled to room temperatureand purified by chromatography, and the product was recrystallized if necessary (chloroform in methanol).

Table 3
Examples 158-187

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
158	4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	3-phenyl-propionaldehyde	IR (KBr) 3340,3240-2800,1600,1580,1540; H. Res. MS *m/z* 398.2343 $(M+H)^+$.
159	4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	3-methyl-butanaldehyde	IR (KBr) 3550,3410,3320, 3240-2800,1605,1580,1560 H. Res. MS *m/z* 350.2357 $(M+H)^+$.
160	4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	pentanaldehyde	IR (KBr) 3450,3300,3200-2800,1660,1610,1580,1540 H. Res. MS *m/z* 350.2354 $(M+H)^+$.
161	4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	4-(4-bromophenyl)-propionaldehyde	IR (KBr) 3500,3300,3200-3000,1650,1615,1580 H. Res. MS *m/z* 478.1429 $(M+H)^+$.
162	4-amino-5-(butyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	*		IR (KBr) 3400,3350,3200-2900,1650,1620,1580,1570 H. Res. MS *m/z* 322.2032 $(M+H)^+$.
163	4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-cyanophenyl-acetaldehyde	IR (KBr) 2850-3550,2220,1610,1580,1560,1540 MS *m/z* 381 $(M+H)^+$.
164	4-amino-5-(2-(N-carbobenzyloxy)aminoethyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-(N-carbobenzyloxy)-aminopropionaldehyde	IR (KBr) 3000-3500,1710,1690,1650,1590 H. Res. MS *m/z* 443.2184 $(M+H)^+$.
165	4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	cycloheptane-carboxaldehyde	IR (KBr) 3500,3250,3100,2950,2850,1620,1575 H. Res. MS *m/z* 362.2349 $(M+H)^+$.
166	4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	**		IR (KBr) 3200-3450,2950-3100,1605,1580,1550 H. Res. MS *m/z* 472.1363 $(M+H)^+$.

167	4-amino-5-(pentyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	hexanal	IR (KBr) 3430,3320,3240-2800,1580,1560,1540,1350; mp. 211-214; MS *m/z* 364 $(M+H)^+$; H. Res. MS *m/z* 364.2506 $(M+H)^+$.
168	4-amino-5-hexyl-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	heptanal	IR (KBr) 3440,3310,3240-2800,1580,1560,1540,1350; mp. 215-217; MS *m/z* 378 $(M+H)^+$; H. Res. MS *m/z* 378.2654 $(M+H)^+$.
169	4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	3-(3-bromophenyl)-propionaldehyde	IR (KBr) 3640-3240,3200-2800,1580,1555,1535,1345; mp. 201-202; MS *m/z* 476/478 $(M+H)^+$; H. Res. MS *m/z* 476.1448 $(M+H)^+$.
170	4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	2-(2-bromophenyl)-acetaldehyde	IR (KBr) 3640-3240,3240-2800,1580,1555,1540,1350; mp. 130-133; MS *m/z* 462/464 $(M+H)^+$; H. Res. MS *m/z* 462.1297 $(M+H)^+$.
171	4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	cyclopropanecarboxaldehyde	IR (KBr) 3490,3290,3240-2760,1610,1580,1540,1375; mp. 235-237; MS *m/z* 462/464 $(M+H)^+$;
172	4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	cyclohexanecarboxaldehyde	IR (KBr) 3640-3000,2980-2760,1610,1580,1540,1345; mp. 231-234; MS *m/z* 462/464 $(M+H)^+$;
173	4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-(2-bromo-5-chlorophenyl)-acetaldehyde	IR (KBr) 3460,3220-2760,1610,1575,1535,1365; mp. 185-187; MS *m/z* 462/464 $(M+H)^+$;
174	4-amino-5-methyl-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	acetaldehyde	IR (KBr) 3640-3250,3250-2760,1610,1585,1560,1350; mp. 238-246; MS *m/z* 462/464 $(M+H)^+$;

* prepared from the compound of Example 157 by reaction with $Pd(PPh_3)_4$ and zinc cyanide in DMF under Suzuki reaction conditions.

** prepared from the compound of Example 173 by reaction with 2-thiopheneboronic acid, $Pd(PPh_3)_4$ and aqueous sodium carbonate under Suzuki reaction conditions.

Examples 175-188

Following the procedures of Example 1, except substituting the appropriate reagents for the R^4 and R^3 reagents of Example 1 as indicated in Table 4 below, compounds of Examples 175-188 were prepared. The treatment with aqueous HCl was omitted, and the free bases were obtained except as indicated.

Table 4

Examples 175-188

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
175	4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2,3-methylenedioxy-benzaldehyde	IR (KBr) 3500-2500,1595,1580,1375; mp. 290-305;
176	4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-fluoro-5-trifluoromethyl-benzaldehyde	IR (KBr) 3500,3440-3240,3200-2800,1610,1580,1560,1540,1370; mp. 293-296; MS *m/z* 428 $(M+H)^+$; H. Res. MS *m/z* 428.1509 $(M+H)^+$.
177	4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-bromo-benzaldehyde	IR (KBr) 3480,3440-3240,3200-2800,1610,1575,1555,1535,1355; mp. 261-263; MS *m/z* 420/422 $(M+H)^+$; H. Res. MS *m/z* 420.0823 $(M+H)^+$.
178	4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3,5-dimethyl-benzaldehyde	IR (KBr) 3480,3440-3240,3200-2800,1610,1575,1555,1535,1360; mp. 284-286; MS *m/z* 370 $(M+H)^+$; H. Res. MS *m/z* 370.2036 $(M+H)^+$.

179	4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3,4-dichloro-benzaldehyde	IR (KBr) 3490,3440-3240,3200-2800,1610,1575,1560,1535,1355; mp. 288-291; MS *m/z* 410/412 $(M+H)^+$; H. Res. MS *m/z* 410.0948 $(M+H)^+$.
180	4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	4-fluoro-3-trifluoromethyl-benzaldehyde	IR (KBr) 3500,3440-3240,3200-2800,1610,1580,1560,1540,1505,1360; mp. 254-257; MS *m/z* 428 $(M+H)^+$; H. Res. MS *m/z* 428.1487 $(M+H)^+$.
181	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)-pyrido[2,3-d]pyrimidine	1-(4-morpholinylphenyl)-ethanone	3-bromo-5-methoxy-benzaldehyde	IR (KBr) 3470,3440-3240,3200-2800,1605,1580,1560; mp. 257-260; MS *m/z* 492/494 $(M+H)^+$.
182	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine	1-(4-pyrrolidinylphenyl)-ethanone	3-bromo-5-methoxy-benzaldehyde	IR (KBr) 3470,3440-3240,3200-2800,1610,1580,1560,1540,1355; mp. d 250; MS *m/z* 476/478 $(M+H)^+$.
183	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)-pyrido[2,3-d]pyrimidine	1-(4-piperidinylphenyl)-ethanone	3-bromo-5-methoxy-benzaldehyde	IR (KBr) 3470,3440-3240,3200-2800,1565; mp. 224-244; MS *m/z* 490/492 $(M+H)^+$;
184	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-bromo-5-methoxy-benzaldehyde	IR (KBr) 3470,3420-3240,3200-2800,1610,1575,1555,1535,1355; mp. 262-266; MS *m/z* 450/452 $(M+H)^+$; H. Res. MS *m/z* 450.0944 $(M+H)^+$.
185	4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-methylthio-benzaldehyde	IR (KBr) 3460,3420-3240,3200-2800,1605,1575,1560,1535,1355; mp. 184-220; MS *m/z* 388 $(M+H)^+$; H. Res. MS *m/z* 388.1586 $(M+H)^+$.

186	4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)-pyrido[2,3-d]pyrimidine	1-(thiophene-2-yl)-ethanone	3-bromo-5-methoxy-benzaldehyde	IR (KBr) 3470,3350-2200,1700,1640,1580,1435,1365,1270; mp. 246-249; MS *m/z* 413/415 $(M+H)^+$; H. Res. MS *m/z* 413.0069 $(M+H)^+$.
187	4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine ***	1-(4-dimethylaminophenyl)-ethanone	2,3-dimethoxy-benzaldehyde	IR (KBr) 3480,3440-3240,3200-2800,1610,1580,1550,1530,1360; mp. 222-225; MS *m/z* 402 $(M+H)^+$; H. Res. MS *m/z* 402.1922 $(M+H)^+$.
188	4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	3-methylsulfonyl-benzaldehyde	IR (KBr)3490,3400-2800,1610,1580,1555,1535,1355; mp. 245~270; MS *m/z* 420 $(M+H)^+$; H. Res. MS *m/z* 420.1493 $(M+H)^+$.

Example 189

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine

A suspension of 4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine (from Example 15, 0.28 g, 0.67 mole) in pyridine (3 mL) was treated with acetic anhydride (0.10 g, 1.0 mmol) and the reaction mixture was stirred for 4 hours at 25 °C. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes) to provide the title compound (0.23 g, 73% theoretical): IR (KBr) 3368, 3048, 1695, 1567; MS *m/z* 462/464 $(M+H)^+$.

Examples 190-198

Following the procedures of Example 189, except substituting the appropriate acylating reagent for the acetic anhydride of Example 189 as indicated in Table 5 below, compounds of Examples 190-198 were prepared.

Table 5

Examples 190-198

Ex. No.	Name	Acylating Reagent	Analytical Data

190	4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine--190	acetic anhydride and formic acid	IR (KBr) 3382, 3047, 1704, 1570; MS *m/z* 448/450 $(M+H)^+$.
191	4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine	methoxyacetyl chloride	IR (KBr) 3344, 3044, 1731, 1561; MS *m/z* 492/494 $(M+H)^+$.
192	4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	trifluoroacetic anhydride	IR (KBr) 3426, 3072, 1610, 1578; MS *m/z* 516/518 $(M+H)^+$.
193	4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	pentanoyl chloride	IR (KBr) 3408, 2954, 1699, 1569; MS *m/z* 504/506 $(M+H)^+$.
194	4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	benzoic anhydride	IR (KBr) 3420, 3056, 1606, 1583; MS *m/z* 524/526 $(M+H)^+$.
195	4-(*N*-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	*N*-BOC-glycyl-imidazole	IR (KBr) 3362, 2975, 1719, 1570; MS *m/z* 577/579 $(M+H)^+$.
196	4-(*N*-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	*N*-phthalimidyl-glycyl-chloride	IR (KBr) 3408, 2927, 1719, 1570; MS *m/z* 607/609 $(M+H)^+$.
197	4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	diethyl dicarbonate	IR (KBr) 3405, 2987, 1738, 1569; MS *m/z* 492/494 $(M+H)^+$.
198	4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)-pyrido[2,3-d]pyrimidine	ethyl isocyanate	IR (KBr) 3405, 3053, 1701, 1548; MS *m/z* 491/493 $(M+H)^+$.

Example 199

4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido [2,3-d] pyrimidine

The product was prepared by treating a solution of 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine in CH_2Cl_2-TEA with allylamine and heating the resulting mixture at reflux for 1 hour. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes) to provide the title compound IR (KBr) 3437, 1564, 1355, 1195; MS *m/z* 460/462 $(M+H)^+$.

The 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido [2,3-d]pyrimidine was prepared as follows.

A sample of 4-(4-bromophenyl)-3-cyano-6-(4-(dimethylamino)phenyl)pyridine-2-amine (from Example 1, 5.0 g, 12.7 mmol) in 20 mL of H_2SO_4 was heated at 80 °C for 30 minutes. Ice was added, and the reaction mixture was neutralized with aqueous NaOH. The resulting crude 3-carboxamide was collected by filtration, triturated with EtOAc-hexanes, then dried under reduced pressure (4.95 g, 95% theoretical). A solution of the carboxamide (4.25 g, 10.3 mmol) in triethylorthoformate (20 mL) was treated with p-toluenesulfonic acid (catalytic) and the reaction mixture was warmed at 80 °C for 4 hours. The volatiles were removed and the crude bicyclic 4-hydroxyl-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidineproduct was suspended in $POCl_3$ (15 mL) then warmed at 100 °C for 2 hours. The $POCl_3$ was removed under reduced pressure to provide crude 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine. The invention therefore relates to intermediate compounds of formula III wherein X is selected from hydroxyl or halogen and the remaining variables are the same as in formula I or II.

Example 200

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido [2,3-d] pyrimidine trihydrochloride

The product was prepared by treating a solution of 4-chloro-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine (prepared as in Example 199) in CH_2Cl_2-TEA with the 2-(dimethylamino)ethylamine and heating the resulting mixture at reflux for 1 hour. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes) to provide the title compound. The product was treated with excess 2M HCl (aq) followed by lyophilization to give the product as the trihydrochloride salt; IR (KBr) 3385, 1561, 1356, 1197; MS *m/z* 491/493 $(M+H)^+$.

Example 201

4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido [2,3-d] pyrimidine tetrahydrochloride

The product was prepared by treating a solution of 4-amino-5-(p-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine in CH_2Cl_2-TEA with the 4-(dimethylamino)butylamine and heating the resulting mixture at reflux for 1 hour. The volatiles were removed under reduced pressure, and the residue was purified by flash chromatography (SiO_2, EtOAc/hexanes). The product was treated with excess 2M HCl (aq) followed by lyophilization to give the product as the

tetrahydrochloride salt; IR (KBr) 3439, 1567, 1356, 1196; MS *m/z* 519/521 $(M+H)^+$.

Example 202

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(p-bromophenyl)pyrido[2,3-d]pyrimidine

A sample of the compound from Example 190 above, 4-formylamino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)-pyrido[2,3-d]pyrimidine (0.27 g, 0.6 mmol) in 3 mL of a 4:1 mixture of THF and DMF at 0°C was treated with NaH (60% dispersion, 36 mg, 0.9 mmol) and the solution was stirred for 0.5 hour. Allyl bromide (0.29 g, 2.4 mmol) was added, and the reaction mixture was stirred for an additional 0.5 hour. Aqueous workup followed by flash chromatography provided the title compound: LRMS *m/z* 488/490. IR (cm^{-1}) 3428, 2910, 1696, 1551, 1362, 1193.

Example 203

4-diacetylamino-5-(4-dimethylaminophenyl)-7-(p-bromophenyl)-pyrido[2,3-d]pyrimidine

This compound was isolated as a minor product from the reaction mixture of Example 190 above: LRMS *m/z* 504/506. IR (cm^{-1}) 2922, 1726, 1550, 1360, 1197.

Example 204

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine

A solution of 5-aminopyridine-2-ethanone (1.15 g, 8.45 mmol), 3-bromobenzaldehyde (1.70 g, 9.2 mmol), malononitrile (0.61 g, 9.2 mmol), and ammonium acetate (1.15 g, 15 mmol) in 25 mL of benzene was heated at reflux with azeotropic removal of water. After 6 hours the reaction mixture was concentrated, and the desired intermediate (1.82 g, 49%) was isolated following flash chromatography (SiO_2, EtOAc-CH_2Cl_2). LRMS *m/z* 366/368. The intermediate was suspended in 15 mL of formamide, and the reaction mixture was heated at 180 °C for 4 hours. The solution was cooled to 25 °C, 10 mL of 4M HCl (aq) was added, and the mixture was stirred for 1 hour. The aqueous solution was neutralized with NaOH (aq), and the precipitate was collected by filtration. The title compound (1.3 g, 68%) was isolated following flash chromatography of the precipitate: LRMS *m/z* 393/395; IR (cm-1) 3481, 3161, 1620, 1573, 1483, 1359.

The 5-aminopyridine-2-carboxaldehyde starting material was prepared as follows:

204a. 5-amino-2-bromopyridine

A solution of 2-bromo-5-nitropyridine (5.1 g, 25 mmol) in 50 mL of a 10:1 mixture of acetic acid and water was treated with iron powder (7.8 g, 140 mmol) in several portions over 20 minutes. After an additional 30 minutes the volatiles were removed under reduced pressure, and the residue was quenched with 5% aqueous sodium carbonate. The aqueous solution was extracted with methylene chloride, and the combined organic layer was dried (sodium sulfate) then concentrated in vacuo to provide the desired product as a white solid (4.25 g, 98%).

204b. 5-aminopyridine-2-ethanone

A sample of 5-amino-2-bromopyridine (4.25 g, 24 mmol), $PdCl_2(PPh_3)_2$ (0.34 g, 2 mole%), CuI (0.09 g, 2 mole%), and trimethylsilylacetylene (3.0 g, 31 mmol) were dissolved in 100 mL of a 4:1 mixture of triethylamine and acetonitrile, and the reaction mixture was stirred 24 hours at 25 °C. The reaction mixture was concentrated, and the residue was dissolved in 100 mL of a 10:1 mixture of acetone and water. $Hg(O_2CCF_3)_2$ (11.1 g, 26 mmol) and H_2SO_4 (72 mmol) were added to the reaction mixture, and the solution was heated at reflux for 2 hours. The reaction mixture was cooled to 25 °C and neutralized with saturated aqueous sodium carbonate. The aqueous layer was extracted with methylene chloride, then the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (SiO2, EtOAc-Hexanes) provided the title compound: LRMS *m/z* 137 (M = H+); IR (cm^{-1}) 3428, 1668, 1646, 1582, 1358, 1274.

Example 205
4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine trihydrochloride salt

Following the procedure of Example 204, 5-dimethylaminopyridine-2-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to give the title compound. The residue was triturated with excess HCl/ether, the volatiles were removed under reduced pressure, and the title compound was dried under high vacuum: LRMS m/z 421/423. IR (cm-1) 3245, 1664, 1545, 1395.

The 5-dimethylaminopyridine-2-carboxaldehyde starting material was prepared as follows:

205a. 3-*N*,*N*-dimethylaminopyridine

A solution of 3-aminopyridine (9.4 g, 0.10 mol) in a 1:1 mixture of formic acid (96%) and formaldehyde (37% aqueous solution) was heated at reflux for 18 hours. The volatiles were removed under reduced pressure and the residue was

neutralized with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, then the combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography (SiO2, EtOAc-Hexanes) provided the title compound: (11.1 g, 91%), LRMS *m/z* 123 (M + H+).

205b. 2-bromo-5-*N*,*N*-dimethylaminopyridine

A solution of 3-*N*,*N*-dimethylaminopyridine (5.88 g, 48.1 mmol) in 150 mL of CH2Cl2 at 0 °C was treated with 2,4,4,6-tetrabromo-2,5-cyclohexadienone (20.7 g, 50 mmol) in several portions over 30 minutes. After 2 hours at 0 °C the reaction mixture was concentrated, and the desired 2-bromo-5-*N*,*N*-dimethylaminopyridine was isolated following flash chromatography (16.5 g, 82%): LRMS *m/z* 201/203.

204c. 5-*N*,*N*-dimethylaminopyridine-2-ethanone

Following the procedure of Example 203b, 2-bromo-5-*N*,*N*-dimethylaminopyridine, except converting the compound to the trihydrochloride salt by treatment with HCl/ether, was converted to the title compound: LRMS *m/z* 165; IR (cm-1) 3480, 1666, 1581, 1368, 1272.

Example 206
4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)-pyrido[2,3-d]pyrimidine hydrochloride

Following the procedure of Example 204, 5-dimethylaminopyrazine-2-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to give the title compound. The residue was triturated with excess HCl/ether, the volatiles were removed under reduced pressure, and the title compound was dried under high vacuum: LRMS m/z 422/424. IR (cm^{-1}) 3310, 1630, 1525, 1444, 1375.

The 5-dimethylaminopyrazine-2-carboxaldehyde starting material was prepared as follows:

206a. 5-dimethylaminopyrazine-2-ethanone

A solution of 5-hydroxypyrazine-2-carboxylic acid (4.0 g, 28.5 mmol) in 50 mL of thionyl chloride and 0.1 mL of DMF was heated at reflux for 8 hours. The volatiles were removed under reduced pressure, and the residue was dissolved in 20 mL of toluene. This solution was added to a solution of dimethyl malonate (4.75 g, 36 mmol), $MgCl_2$ (2.09 g, 22 mmol) and triethyl amine (7.08 g, 70 mmol) in 100 mL of toluene. The reaction mixture was stirred for 1 hour at 25 °C, quenched by addition of water, and the product was extracted with methylene chloride. The solvent was

removed, the crude intermediate was dissolved in 25 mL of a 25:1 mixture of DMSO and water, and the resulting solution was warmed at 150 °C for 2 hours. The reaction was quenched by addition of water, and the product was extracted with methylene chloride to provide 2-acetyl-5-chloropyrazine (LRMS *m/z* 156). This intermediate was treated with aqueous dimethylamine at room temperature for 30 minutes to afford 5-dimethylaminopyrazine-2-ethanone (LRMS *m/z* 166): LRMS m/z 422/424; IR (cm^{-1}) 3310, 1630, 1525, 1444, 1375.

Example 207

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine

Following the procedure of Example 204, 2-oxobenzoxazolin-6-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to prepare the title compound: LRMS m/z 434/436; IR (cm^{-1}) 3095, 1760, 1579, 1481, 1350.

The 2-oxobenzoxazolin-5-ethanone starting material was prepared as follows:

207a. 2-oxobenzoxazolin-6-ethanone

DMF (9 mL) was added dropwise to $AlCl_3$ (58.7 g, 440 mmol) over 20 minutes and the resulting suspension was stirred 15 minutes at 25 °C. Acetic anhydride (7.14 g, 70 mmol) and 2-benzoxazolinone (6.0 g, 44 mmol) were added and the reaction mixture was warmed at 80 °C and stirred for 4 hours. The mixture was cooled to 25 °C and poured into ice/H_2O. The resulting precipitate was collected by filtration and dried under vacuum to provide the title compound (6.4 g, 81%, LRMS *m/z* 177).

Example 208

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)-pyrido[2,3-d]pyrimidine

Following the procedure of Example 204, 1-methyl-2-oxobenzoxazolin-5-ethanone was reacted with bromobenzaldehyde, malononitrile, and ammonium acetate to prepare the title compound: LRMS m/z 448/450; IR (cm^{-1}) 3440, 1782, 1605, 1458, 1350.

The 1-methyl-2-oxobenzoxazolin-5-ethanone starting material was prepared as follows:

208a. 1-methyl-2-oxobenzoxazolin-5-ethanone

A solution of 2-oxobenzoxazolin-5-ethanone (from Example 206a, 2.50 g, 14.1 mmol) in 20 mL of a 4:1 mixture of THF and DMF at 0 °C was treated with NaH (60 % dispersion, 0.8 g, 20 mmol) and the mixture was stirred 20 minutes at 0 °C. Methyl iodide (3.97 g, 28 mmol) was added and the reaction mixture was warmed to 25 °C and stirred for 15 minutes. Saturated aqueous $NaHCO_3$ was added and the aqueous layer was extracted with CH_2Cl_2. The desired product (2.55 g, 94%, LRMS *m/z* 191), was isolated following flash chromatography (SiO_2, EtOAc-CH_2Cl_2).

Example 209

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 173 by reaction with 3-methoxyphenylboronic acid, $Pd(PPh_3)_4$ and aqueous sodium carbonate under Suzuki reaction conditions. IR (KBr) 3550-3250,3240-2760,1580,1560,1540,1350; H. Res. MS m/z 496.1902 $(M+H)^+$.

Example 210

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 157, except substituting 1-(4-dimethylaminophenyl)-ethanone for the R^4 reagent and 2-(2-bromophenyl)-acetaldehyde for the R^3 reagent of Example 157, the title compound was prepared as shown in Table 6.

Table 6

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
210	4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-(2-bromophenyl)-acetaldehyde	IR (KBr); MS m/z 434,436 $(M+H)^+$.

Example 211

4-amino-5-(2-((thiophene-2-yl)phenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 173 by reaction with 2-thiopheneboronic acid, $Pd(PPh_3)_4$ and aqueous sodium carbonate under Suzuki reaction conditions. IR (KBr) 3640-3240, 3240-2800, 1580, 1560, 1540, 1350; H. Res. MS m/z 466.2070 $(M+H)^+$.

Example 212

4-amino-5-(2-((thiophene-3-yl)phenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 173 by reaction with 3-thiopheneboronic acid, $Pd(PPh_3)_4$ and aqueous sodium carbonate under Suzuki reaction conditions. IR (KBr) 3640-3240, 3240-2800, 1580, 1560, 1540, 1350; H. Res. MS m/z 466.2057 $(M+H)^+$.

Examples 213-222

Following the procedures of Example 1, except substituting the appropriate reagents for R^4 and R^3 as indicated in Table 7 below, compounds of Examples 212-222 were prepared.

Table 7

Examples 213-222

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
213	4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-formyl-N-(2-methoxy)ethylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3490, 1689, 1120, 800 cm^{-1}; MS *m/z* 478/480 $(M+H)^+$.
214	4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	*		IR (KBr) 3330,2925, 1675, 800 cm^{-1}; MS *m/z* 451/453 $(M+H)^+$.
215	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3440, 1600, 1160, 810 cm^{-1}; MS *m/z* 477/479 $(M+H)^+$.
216	4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;	**		IR (KBr) 3480, 1520, 710 cm^{-1}; MS *m/z* 464,466 $(M+H)^+$.

217	4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;	***		IR (KBr) 3475, 1690, 1355, 800 cm^{-1}; MS *m/z* 420/422 $(M+H)^+$.
218	4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;	****		IR (KBr) 3452, 1605, 1250, 590 cm^{-1}; MS *m/z* 477/479 $(M+H)^+$.
219	4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(2-oxo-3-oxazolidinyl)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3480, 1750, 1400, 700 cm^{-1}; MS *m/z* 462/464 $(M+H)^+$.
220	4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-(6-(2-propyl)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3474, 3098, 1636, 1566, 1499, 1352, 1282 cm^{-1};MS *m/z* 393 $(M+H)^+$.
221	4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine dihydrochloride	1-(3-methyl-4-pyrrolidinylphenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3440, 1640, 1607, 1586, 1370 cm^{-1}; MS *m/z* 433 $(M+H)^+$.
222	4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-(6-imidazolyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3028, 1641, 1607, 1595, 1375cm^{-1}; MS *m/z* 417 $(M+H)^+$.

*prepared by deformylation of Example 213 with dilute HCl in methanol.

**prepared by acylation of Example 213 with 2-methoxyacetyl chloride/pyridine.

***prepared by formylation of the 7-(3-bromophenyl)-2-cyano-5-(4-aminophenyl)pyridine-2-amine intermediate.

****prepared by acylation of Example 213 with the 2-(dimethylamino)acetyl chloride.

Examples 223-225

Following the procedures of Example 157, except substituting the appropriate reagents for the R^4 and R^3 reagents of Example 157 as indicated in Table 8 below, compounds of Examples 223-225 were prepared.

Table 8

Examples 223-225

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
223	4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	1-(4-diethylaminophenyl)-ethanone	2-phenyl-acetaldehyde	IR (KBr) 3450,3380,2850-3200,1605,1580,1560,1540; H. Res. MS *m/z* 384.2176 $(M+H)^+$.
224	4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine	*		IR (KBr) 2400-3450,2050,2120,1650,1605,1540; MS *m/z* 437 $(M+H)^+$.
225	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine	1-(4-dimethylaminophenyl)-ethanone	2-(2-bromophenyl)-)propionaldehyde	IR (KBr) 3520,3250-3500,2850-3150,1605,1580,1560,1540; H. Res. MS *m/z* 448.1137 $(M+H)^+$.

*prepared from the compound of Example 170 by reaction with propargylamine, CuI and $Pd(PPh_3)_4$ under Suzuki reaction conditions.

Examples 226-228

Following the procedures of Example 1, except substituting the appropriate reagents for R^4 and R^3 as indicated in Table 9 below, compounds of Examples 226-228 were prepared.

Table 9

Examples 226-228

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
226	4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine	1-(4-bromophenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3456, 3053, 16600, 1556 cm^{-1}; MS *m/z* 420 $(M+H)^+$.
227	4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)-pyrido[2,3-d]pyrimidine	1-(4-(N-morpholinyl)phenyl)ethanone	furan-2-carboxaldehyde	IR (KBr) 3460, 1600, 1580, 1457 cm^{-1}; MS *m/z* 374 $(M+H)^+$.

228	4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine	1-(5-(2-(dimethylamino)pyrimidinyl))ethanone	3-bromo-benzaldehyde	IR (KBr) 3442 1640, 1604, 1577, 1536, 1408, 1367, 1348 cm^{-1}; MS *m/z* 422 $(M+H)^+$.

Example 229

4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine

A solution of 4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine (Example 71, 310 mg, 0.79 mmol) in 2 mL of acetic acid was treated with sodium cyanate (56 mg, 0.87 mmol), and the reaction mixture was stirred for 30 minutes at 25 °C. The solution was concentrated and the residue was suspended in aqueous $NaHCO_3$. The crude product was collected by filtration, then purified by flash chromatography. The product was dissolved in methanol and treated with excess 2M aqueous HCl to provide the hydrochloride salt: LRMS m/z 435/437. IR (cm^{-1}) 3442, 2212, 3186, 3059, 1681, 1582, 1525, 1358.

Example 230

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 157, except substituting 1-(4-diethylamino-phenyl)-ethanone for the R^4 reagent and 1-phenylmethylpiperidine-3-carboxaldehyde (prepared as described by Gilligan *et al., J. Med. Chem.*, 35:4344-4361 **(1992)**) for the R^3 reagent thereof, the title compound was prepared. The treatment with aqueous HCl was omitted, and the free base was obtained. IR (KBr) 3440, 3100-2800-1640, 1605, 1595, 1535 cm^{-1}; MS *m/z* 467 $(M+H)^+$; mp 218-220 °C.

Examples 231-243

Following the procedures of Example 1, except substituting the appropriate reagents for R^4 and R^3 as indicated in Table 10 below, compounds of Examples 230-243 were prepared. In some cases, the treatment with aqueous HCl was omitted, and the free bases were obtained.

Table 10
Examples 231-243

Ex. No.	Name	R^4 Reagent (for 7-position)	R^3 Reagent (for 5-position	Analytical Data
231	4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1635, 1574, 1562, 1352 cm^{-1}; MS *m/z* 459 $(M+H)^+$.
232	4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-chloro-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3478, 1608, 1574, 1542 cm^{-1}; MS *m/z* 414 $(M+H)^+$.
233	4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-methoxy-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3484, 1635, 1560, 1348 cm^{-1}; MS *m/z* 409 $(M+H)^+$.
234	4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3494, 1612, 1579, 1467, 1359, 1271, 1233 cm^{-1}; MS *m/z* 445 $(M+H)^+$.
235	4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;	1-(2-morpholinyl-5-pyrimidinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3434, 1637, 1608, 1585, 1335, cm^{-1}; MS *m/z* 463 $(M+H)^+$.
236	4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;	1-(4-pyrrolidinylphenyl)-ethanone	2-thiazole-carboxaldehyde	IR (KBr) 3400, 1637, 1608, 1532, cm^{-1}; MS *m/z* 376 $(M+H)^+$.
237	4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl))-pyrido[2,3-d]pyrimidine;	1-(6-pyrazolyl-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3474, 1580, 1562, 1492, 1395, cm^{-1}; MS *m/z* 444 $(M+H)^+$.
238	4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;	1-(4-(1-methyl-ureido)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3400, 1665, 1350 cm^{-1}; MS *m/z* 450 $(M+H)^+$
239	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3475, 1578, 1553, 1482, 1396, cm^{-1}; MS *m/z* 484 $(M+H)^+$.

240	4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine; *	1-(3-fluoro-4-(N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3448, 1600, 1525, 1476, cm^{-1}; MS *m/z* 484 $(M+H)^+$.
241	4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine; *	1-(3-fluoro-4-(N-methylamino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3465, 1607, 1546, 1350, cm^{-1}; MS *m/z* 481 $(M+H)^+$.
242	4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)-phenyl)pyrido[2,3-d]pyrimidine;	1-(4-(N-methyl-N-methylsulfonyl-amino)phenyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3470, 1650, 1570, 1338, cm^{-1}; MS *m/z* 484 $(M+H)^+$.
243	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;	1-(6-(N-methyl-N-methylsulfonyl-amino)-3-pyridinyl)-ethanone	3-bromo-benzaldehyde	IR (KBr) 3460, 1680, 1580, 1330 cm^{-1}; MS *m/z* 485 $(M+H)^+$.

* separated by chromatography from the same reaction mixture; formylation occurs during the cyclization step

Example 244

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine dihydrochloride

A sample of 4-(3-bromophenyl)-3-cyano-6-(1-methyl-5-indolinyl)pyridine-2-amine was heated at reflux in formamide. The reaction was monitored by TLC, and when the reaction was complete the mixture was cooled to room temperature. The product was allowed to precipitate, then recovered by filtration and washed with water. Additional product was extracted from the filtrate. The product was purified by column chromatography eluting with 10% $MeOH/CH_2Cl_2$ and converted to the hydrochloride salt by treatment with ether/HCl. The salt was isolated and dried under vacuum to give the title compound. LRMS m/z 432/434; IR (cm^{-1}) 3500, 3400, 3300, 3200-2800, 1610, 1580, 1560, 1540.

The 4-(3-bromophenyl)-3-cyano-6-(1-methyl-5-indolyl)pyridine-2-amine starting material was prepared as follows:

244a. 5-bromo-1-methylindoline

Acetic acid (60 mL) was added to a mixture of 5-bromo-1-methylindole (10 g, 47.6 mmol) and sodium cyanoborohydride (8 g). After one hour at 15 °C, the reaction was basified with aqueous NaOH and extracted with toluene. The organic phase was dried over $MgSO_4$ and concentrated to a powder under vacuum. This material was purified by flash chromatography to give the title compound, 8.62 g (82 %): MS 212, 214 $[M+H]^+$.

244b. 5-acetyl-1-methylindoline

A mixture of 5-bromo-1-methylindoline (8.6 g, 40.7 mmol), trimethylsilylacetylene (12 mL), palladium bis-triphenylphosphine dichloride (600 mg), CuI (620 mg) and triethylamine (16 mL) in acetonitrile (20 mL) was heated at 75 °C for 3 days, then cooled and concentrated *in vacuo*. The residue was dissolved in 120 mL of 1:1 ethyl acetate/hexane, and the solids were removed by filtration. The solvent was removed and a sample of the residue (5 g) was dissolved in 90% aqueous acetone (44 mL). To this solution was added sulfuric acid (2.2 g), and $Hg(OCOCF_3)_2$ (9 g). The reaction was heated at reflux for 20 minutes, cooled, made basic with aqueous sodium hydroxide and extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and concentrated to an oil, which was purified by flash chromatography to give 850 mg of the title compound: MS 176 $[M+H]^+$.

244c. 4-(3-bromophenyl)-3-cyano-6-(1-methyl-5-indolinyl)pyridine-2-amine

Prepared by condensation of 1',1'-dicyano-3-bromostyrene (prepared by condensation of 3-bromobenzaldehyde with malononitrile in ethanol in the presence of a catalytic amount of glycine) and the 5-acetyl-1-methylindoline (the R^4 reagent) with ammonium acetate in ethanol. The reaction mixture was heated to reflux in a vessel fitted with a Dean-Stark apparatus. After 3.5 hours, the mixture was cooled, and the solvent was removed. The residue was purified by flash chromatography, eluting with methylene chloride, to give the title compound (588 mg, 30% yield; MS m/z 394 $(M+H)^+$.

Example 245

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine tetrahydrochloride

The title compound was prepared according to the procedure of Example 1, except substituting 1-methyl-5-acetyl-benzimidazole (prepared according to the procedure of D. J. Evans *et. al., J. Chem. Soc. Perkin Trans. II*, **1978**, 865) for the 4-

dimethylaminobenzaldehyde (the R^3 reagent) therein. IR (KBr) 3650-3230, 3230-2000, 1635, 1605, 1590, 1555, 1365 cm^{-1}; MS *m/z* 431/433, 431.0605 $(M+H)^+$.

Example 246

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine tetrahydrochloride

246a. 6-(1-butoxyethenyl)-3-chloropyridazine

To a solution of 20 g (200 mmol) of butyl vinyl ether in 80 mL of THF at -78 °C was added 130 mL of a 1.7 M solution of t-butyl lithium in pentane over about 20 minutes. The yellow suspension was stirred while allowing to warm to 0 °C. THF (150 mL) was added, and the mixture cooled to -78 °C and a solution of 23 mL (200 mmol) of trimethyl borate in 50 mL of THF was added. The reaction was warmed to 20 °C, 20 mL of methanol was added, and the solution concentrated in vacuo. The residue was diluted with 400 mL of dioxane, and 20.9 g (140 mmol) of 3,6-dichloropyridazine, 2.31 g of $Pd(PPh_3)_4$, and 200 mL of 2 M- aqueous sodium carbonate was added. The reaction was heated to reflux over one hour, then cooled and filtered to remove solids. The filtrate was concentrated in vacuo and partitioned between ethyl acetate and 1 M sodium hydroxide. The organic phase was dried over Na_2SO_4, concentrated in vacuo, and purified by flash chromatography to give 6.3 g (21%) of the title compound. MS {M +]+ 213, 215.

246b. 1-(6-chloropyridazin-3-yl)ethanone

A mixture 6.3 g of the compound from Step 246a in 40 mL of dimethoxyethane, 10 mL of water, and 4 mL of 12 M HCl was stirred for 20 minutes, then 125 mL of water was added, and the reaction was neutralized with 12 g of $NaHCO_3$. The reaction was extracted with ethyl acetate, dried over Na_2SO_4, and concentrated *in vacuo* to give a yellow solid, 4.7 g.

246c. 1-(3-(6-(dimethylamino)pyridazin-3-yl))ethanone (the R^4 reagent)

A solution of 1.57 g (10 mmol) of 1-(6-chloropyridazin-3-yl)ethanone (from Step 246b) in 15 mL of dimethoxyethane was treated with 50 mmol of 40% aqueous dimethylamine. After one hour, the reaction was partitioned between CH_2Cl_2 and water. The organic phase was dried over CH_2Cl_2 , and concentrated *in vacuo* to give the title compound.

246d. 3-acetyl-6-(dimethylamino)pyridazine

The title compound was prepared by condensing 1,1-dicyano-(3-(3-bromophenyl)propene (the R^3 reagent) with the compound from Step 246c (the R^4 reagent) and ammonium acetate in ethanol according to the procedure of Example 157d.

246e. 4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine tetrahydrochloride

The title compound was prepared from the compound of Step 246d according to the procedure of Example 157, except substituting formamide for the ammonium sulfate and triethyl orthoformate thereof.

Examples 247-248

Following the procedures of Example 246, except in step (c) substituting the appropriate reagents for methylamine as indicated in the Table 11A below, compounds of Examples 247-248 were prepared.

Table 11A
Examples 247-248

Ex. No.	Name	reagent of step c	Analytical Data
247	4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	morpholine	IR (KBr) 3600-3200, 3000, 1630, 1605, 1590, 1550 cm^{-1}; MS *m/z* 464/466, 464.0829 $(M+H)^+$;
248	4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	pyrrolidine	IR (KBr) 3600-3250, 3100-2800, 1640, 1605, 1560 cm^{-1}; MS *m/z* 448/450, $(M+H)^+$;

Examples 249-251

Following the procedures of Example 244, except in step (c) first substituting the appropriate reagent for R^4 as indicated in Table 11B below for the R^4 reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds of Examples 249-251 were prepared. In some cases, the hydrochloride salts were not prepared.

Table 11B
Examples 249-260

Ex. No.	Name	R^4 Reagent (for 7-position)	Analytical Data
249	4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	2-acetyl-5-morpholinyl-pyrazine	IR (KBr) 3478, 3058, 1562, 1542, 1378, 1306 cm^{-1}; MS *m/z* 464/466, $(M+H)^+$;
250	4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine dihydrochloride	2-acetyl-5-(N-(2-methoxyethyl)-N-methylamino)-pyrazine	IR (KBr) 3482, 3299, 3053, 1612, 1540, 1310 cm^{-1}; MS *m/z* 466/468, $(M+H)^+$;
251	4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine hydrochloride	1-((4-acetylphenyl)-methyl)-morpholine	IR (KBr) 3040, 1680, 1640, 1605, 1580, 1400 cm^{-1}; MS *m/z* 466/468, $(M+H)^+$;

Example 252

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride

Step 252a. 1-(5-bromo-2-pyridyl)ethanone, ethylene ketal

A solution of dibromopyridine (5.2 g, 21.95 mmol), tributyl(1-ethoxyvinyl)tin (9.11 g, 25.24 mmol), $Pd_2(dba)_3$ (0.7 g, 0.8 mmol), and $(2\text{-furyl})_3P$ (0.37 g, 1.6 mmol) in 50 mL of toluene/THF (5:1) was warmed at reflux for 10 hours. The reaction mixture was concentrated, and the crude product was purified by elution through a short column of silica gel. The resulting enol-ether compound, ethylene glycol (2.79 g, 45 mmol), and *p*-toluene sulfonic acid (0.1 g) were dissolved in 50 mL of toluene and the solution was warmed at reflux for 10 hours. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried (Na_2SO_4), concentrated under reduced pressure, and the resulting crude product was purified by flash chromatography to provide the title compound (3.68 g, 79%).

Step 252b. 1-(5-(bis(2-methoxyethyl)amino)-2-pyridyl)ethanone

Following literature procedure (*J. Org. Chem.* **1996**, *61*, 720), a suspension of the compound from step 252a, bis(2-methoxyethyl)amine, *t*-BuONa, $Pd_2(dba)_3$, and BINAP toluene was warmed at 80 °C for 8 hours. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was concentrated and the resulting residue was dissolved in 20 mL THF/3 M HCl (4:1) and stirred for 4 h. The reaction mixture was neutralized by the addition of 2 M NaOH (aq) and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried, concentrated under reduced pressure, and the crude product was purified by flash chromatography to provide the title compound

Step 252c. 4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride

Following the procedures of Example 244, except in step (c) first substituting the reagent from Step 252b for the R^4 reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the free base of the title compound was prepared. The title compound was prepared from this by treatment with HCL in ether. IR (KBr) 3440, 1635, 1605, 1580, 1360 cm^{-1}; MS *m/z* 466/468, $(M+H)^+$.

Examples 253-260

Following the procedures of Example 244, except in step (c) first substituting the appropriate reagent for R^4 as indicated in Table 11B below for the R^4 reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds of Examples 253-260 were prepared. In some cases, the hydrochloride salts were not prepared.

Ex. No.	Name	R^4 Reagent (for 7-position)	Analytical Data
253	4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-((4-acetylphenyl)-methyl)imidazole	IR (KBr) 3105, 1645, 1620, 1570, 1350 cm^{-1}; MS *m/z* 466/468, $(M+H)^+$;

254	4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine trihydrochloride	1-(5-morpholinyl-2-pyridyl)ethanone *	IR (KBr) 3297, 3081, 1646, 1564, 1494, 1362 cm^{-1}; MS *m/z* 463/465, $(M+H)^+$;
255	4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine dihydrochloride	1-(4-((dimethylamino)methyl)phenyl)-ethanone	IR (KBr) 3308, 1645, 1590, 1560, 1375 cm^{-1}; MS *m/z* 509/511, $(M+H)^+$;
256	4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine dihydrochloride	1-(5-(4-hydroxypiperidinyl)-2-pyridyl)ethanone **	IR (KBr) 3000, 1650, 1600, 1580, 1550, 1400 cm^{-1}; MS *m/z* 477/479, $(M+H)^+$;
257	4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine dihydrochloride	5-acetyl-2-pyridinemethanamine	IR (KBr) 3477, 3060, 1678, 1638, 1566, 1495, 1319 cm^{-1}; MS *m/z* 435/437, $(M+H)^+$;
258	4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine	2-acetyl-5-(2-propenyl)-pyridine	IR (KBr) 3085, 1562, 1485, 1357 cm^{-1}; MS *m/z* 418/420, $(M+H)^+$;
259	4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine hydrochloride	6-acetyl-3-(2-methoxyethyl)-benzoxazol-2-one	IR (KBr) 3440, 1770, 1625, 1605, 1580, 1360 cm^{-1}; MS *m/z* 492/494, $(M+H)^+$;
260	4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine	4-acetylbenzeneethanamine	IR (KBr) 3283, 3054, 1678, 1631, 1547, 1352 cm^{-1}; MS *m/z* 448/450, $(M+H)^+$;

* Prepared as in Ex. 252b, except substituting morpholine for the bis(2-methoxyethyl)amine thereof.

** Prepared as in Ex. 252b, except substituting 4-hydroxypiperidine for the bis(2-methoxyethyl)amine thereof.

Example 261

4-amino-5-(3-pyridyl)-7-(4-dimethylamino)phenylpyrido[2,3-d]pyrimidine

The compound was prepared by using the method generally described above in Scheme 3 and the associated examples using 1-(4-dimethylaminophenyl)ethanone as the R^4 reagent (7-position) and nicotinaldehyde as the R^3 reagent (5-position). IR (cm-1) 3305.8, 2922, 1606, 1578, 1535, 1360. MS (M+H) 342.

Example 262

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride

The title compound was prepared by using the method described in Example 200, except substituting methylamine for the 2-(dimethylamino)ethylamine thereof. MS (M+H), 478 (1Br); IR (cm-1) 3455, 3047, 2959, 1580, 1351, 1234.

Example 263

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride

The title compound was prepared by using the method described in Example 200, except substituting 2-methoxyethylamine for the 2-(dimethylamino)ethylamine thereof. MS (M+H), 522 (1Br); IR (cm-1) 3415, 2920, 1569, 1321, 1234.

Example 264

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride

Step 264a. 1-(4-(1-Methylimidazol-2-yl)phenyl)ethanone

A solution of *N*-methyl imidazole (0.90 g, 11.0 mmol) in 12 mL of THF at -78 °C was treated with *n*-BuLi (7.5 mL, 1.6 M solution in hexanes, 12.0 mmol) for 0.5 hours at -78 °C. Next, $ZnCl_2$ (20 mL, 1.0 M solution in Et_2O, 20 mmol) was added, and the solution was warmed to 25°C. To this solution was added $Pd(PPh_3)_4$ (70 mg, 0.06 mmol) followed by 4-iodoacetophenone ethylene acetal (prepared from iodoacetophenone and ethylene glycol in the presence of an acid catalyst by standard procedures), and the reaction mixture was heated at reflux for 4 hours. The solution was then cooled to 25 °C and quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was concentrated under reduced pressure. The residue was dissolved in 30 mL of THF, 15 mL of 3 M aqueous HCl was added, and the mixture was stirred for 2 hours at 25 °C. The solution was neutralized by the addition of saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) then concentrated under reduced pressure. The crude product was purified by flash chromatography to provide the title compound (0.89 g, 64%).

Step 264b. 4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride

Following the procedures of Example 244, except in step (c) first substituting the R^4 reagent from Step 264a for the R^4 reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 458 (1Br); IR (cm-1) 3051, 2948, 1577, 1474, 1354.

Examples 265-267

Following the procedures of Example 244, except in step (c) first substituting the appropriate reagent for R^4 as indicated in the Table below for the R^4 reagent of Example 244 step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds of Examples 264-285 were prepared. In Ex. 266, the hydrochloride salt was not prepared.

Ex. No.	Name	R^4 Reagent (for 7-position)	Analytical Data
265	4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine	1-(4-(aminomethyl)phenyl)ethanone	MS (M+H), 460; IR (cm-1) 3024 2933, 1550, 1493, 1328
266	4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine	1-(2-bromo-4-(dimethylamino)phenyl)ethanone	MS (M+H), 500 (2 Br); IR (cm-1) 3049, 2949, 1536, 1468, 1320
267	4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine	1-(4-(dimethylaminoethyl)phenyl)ethanone	MS (M+H), 448 (1 Br); IR (cm-1) 3420, 3000, 2980, 1635, 1610, 1590, 1435, 1415

Example 268

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine

A suspension of the compound of Example 63 (0.80 g, 1.59 mmol), $PdCl_2(PPh_3)_2$, CuI, and 3-dimethylaminoprop-1-yne in 20 mL of DMF/TEA (4:1) was heated at 50 °C for 3 hours. The volatiles were removed under reduced pressure, and the

residue was purified by flash chromatography to provide the title compound (0.50 g, 68 %). MS (M+H), 459 (1Br); IR (cm-1) 3027, 2964, 1513, 1470, 1360.

Examples 269-271

Following the procedures of Example 268, except substituting the reagent compound shown in the table below for the 3-dimethylaminoprop-1-yne of Example 268, the compounds shown in the table below were prepared.

Ex. No.	Name	Reagent	Analytical Data
269	4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine	1,1-dimethyl-propargyl amine	MS (M+H), 459 (1Br); IR (cm-1) 3041, 2967, 1562, 1484, 1319
270	4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine	dimethyl phosphite	MS (M+H), 486 (1Br); IR (cm-1) 3105, 2912, 1625, 1437, 1350
271	4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine	methyl propargyl ether	MS (M+H), 446 (1Br); IR (cm-1) 3053, 2929, 1560, 1484, 1352

Example 272

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine

A solution of 4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine (the compound of Example 37, (0.47 g, 1.17 mmol) in 15 mL of 6 M HCl (aqueous) was heated at 60 °C for 8 hours. The mixture was lyophilized and the crude product was purified by flash chromatography to provide the title compound (0.14 g, 28%). MS (M+H), 422 (1Br); IR (cm-1) 3064, 2628, 1692, 1403, 1273.

Example 273

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazinyl)pyrido[2,3-d]pyrimidine

Step 273a. 7-acetyl-2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one

A solution of 2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one (9.8 g, 65.27 mmol, Aldrich) in 120 mL of THF/MeOH (5:1) was treated with 0.4 mL of concentrated HCl (aqueous) followed by N-bromosuccinimide (17.8 g, 100 mmol) in several portions over 10 minutes. After 12 hours at 25 °C the reaction mixture was quenched by the addition of

saturated aqueous $NaHSO_3$. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was dried (Na_2SO_4), concentrated under reduced pressure, and purified by flash chromatography to provide 7-bromo-2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one (8.4 g, 56%). A mixture of 7-bromo-2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one (3.2 g, 14 mmol), tributyl(1-ethoxyvinyl)tin (6.1 g, 17 mmol), $Pd_2(dba)_3$ (0.5 g, 0.56 mmol), and (2-furyl)$_3$P (0.3 g, 1.2 mmol) in 30 mL of toluene/THF (5:1) was warmed at reflux for 10 hours. The reaction mixture was concentrated under reduced pressure, and the residue was dissolved in 50 mL of THF. 15 mL of 4 M HCl (aqueous) was added, and the mixture was stirred for 4 hours at 25 °C. The solution was neutralized by the addition of $NaHCO_3$ (aqueous), and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried (Na_2SO_4), concentrated, and the crude product was purified by flash chromatography to provide 7-acetyl-2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one (2.37 g, 88%). MS (M+H), 463 (1 Br); IR (cm-1) 3400, 3200-2800, 1700, 1640, 1605, 1590, 1395, 1380, 1345.

Step 273b. 7-acetyl-4-methyl-2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one

The compound from step 273 a was treated with methyl iodide and NaH in 1:1 THF/DMF for 6 hours at 0 °C to 25 °C. The reaction was quenched with aqueous sodium bicarbonate solution, the mixture was extracted with dichloromethane, and the resiue was purified by chromatogaphy to give the title compound. MS (M+H), 407.

Step 273c. 4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazinyl)pyrido[2,3-d]pyrimidine

Following the procedure of Example 244 Step c, except first substituting 7-acetyl-4-methyl-2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one (the R^4 reagent) from Step 273b for the R^4 reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H), 463 (1 Br); IR (cm-1) 3400, 3200-2800, 1700, 1640, 1605, 1590, 1395, 1380, 1345.

Example 274

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Step 274a. 7-acetyl-4-dimethylaminoethyl -2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one

The compound from Example 273 Step a was treated with 2-chloro-(N,N-dimethyl)ethylamine HCl and K_2CO_3 in aqueous acetone at reflux. The mixture was diluted with water and extracted with dichloromethane, and the residue was purified by chromatogaphy to give the title compound.

Step 274b. 4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting 7-acetyl-4-dimethylaminoethyl -2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one (the R^4 reagent, from Step 273b) for the R^4 reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H), 519 (1 Br); IR (cm-1) 3440, 1685, 1630, 1605, 1580, 1395

Example 275

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine

Step 275a. 6-acetyl-2-benzoxazolinone

Following the procedures of Example 273 Step a, except substituting 2-benzoxazolinone (Aldrich) for the 2*H*-pyrido[3,2-b]-1,4-oxazin-3(4*H*)-one thereof, the title compound was prepared.

Step 275b. 6-acetyl-3-(dimethylaminoethyl)-2-benzoxazolinone

The compound from Example 275 Step a was treated with 2-chloro-(N,N-dimethyl)ethylamine HCl and K_2CO_3 in aqueous acetone at reflux. The mixture was diluted with water and extracted with dichloromethane, and the residue was purified by chromatogaphy to give the title compound.

Step 275c. 4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting the compound from Step 275a for the R^4 reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H), 506 (1 Br); IR (cm-1) 3400, 3050, 1630, 1610, 1360.

Example 276

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Step 276a. 6-acetyl-3-methyl-2-benzoxazolinone

The compound from Example 275 Step a was treated with methyl iodide and NaH in 1:1 THF/DMF for 6 hours at 0 °C to 25 °C. The reaction was quenched with aqueous sodium bicarbonate solution, the mixture was extracted with dichloromethane, and the resiue was purified by chromatogaphy to give the title compound.

Step 276b. 1-(3-hydroxy-4-methylaminophenyl)-ethanone

The compound from Step 276a (1.60 g, 8.37 mmol) was dissolved in acetone (70 mL) and treated with 1M aqueous K_2CO_3 solution (25 mL) with heating at reflux overnight. The mixture was neutralized with acid, then extracted with diethyl ether. The solvent was dried ($MgSO_4$) and removed under vacuum to give the title compound (2.01 g)

Step 276c. 7-acetyl-4-methyl-2H-4H-benzo-1,4-oxazin-3-one

The compound from Step 276b (2.01 g, 8.37 mmol) was dissolved in DMSO and treated with sodium ethoxide (8.4 mmol) and bromoacetic acid (1.40 g, 8.4 mmol) at room temperature overnight. The mixture was diluted with water and ether, and the title compound was isolated by filtration (0.48 g). MS (M+H), 206.

Step 276d. 4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting the compound from Step 276c for the R^4 reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H), 462 (1 Br); IR (cm-1) 3500, 2800-3200, 1690, 1645, 1610, 1590, 1385, 1355.

Example 277

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Step 277a. 7-acetyl-2,2,4-trimethyl-2H-4H-benzo-1,4-oxazin-3-one

The compound from Step 276b (2.25 g, 9 mmol) was dissolved in DMSO and treated with sodium ethoxide (9 mmol) and 2-bromo-2-methylpropanoic acid (1.76 g, 9 mmol) at room temperature overnight. The mixture was diluted with water, and the mixture was extracted with ether.ethyl acetate. The extract was dried ($MgSO_4$), the solvent was removed under vacuum, and the residue was purified by chromatography (silica gel) to give the title compound (1.33 g) MS (M+H), 234.

Step 277b. 4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting the compound from Step 277a for the R^4 reagent of Example 244 Step c, and secondly performing the condensation with ammonium acetate substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H), 490 (1 Br); IR (cm-1) 3450, 2900-3100, 1680, 1645, 1610, 1515, 1385, 1365, 1165.

Example 278

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Step 278a. 1-(3-hydroxy-4-(2-(dimethylamino)ethyl)phenyl)-ethanone

A sample of 6-acetyl-3-(dimethylaminoethyl)-2-benzoxazolinone (from Example 275 Step b) was dissolved in acetone and treated with 1M aqueous K_2CO_3 solution with heating at reflux overnight. The mixture was neutralized with acid, then extracted with diethyl ether. The solvent was dried ($MgSO_4$) and removed under vacuum to give the title compound.

Step 278b. 7-acetyl-4-(dimethylamino)ethyl)-2H-4H-benzo-1,4-oxazin-3-one

A sample of the compound from Step 278a (8.94 g, 32 mmol) was dissolved in DMSO and treated with sodium ethoxide (32 mmol) and bromoacetic acid (5.34 g, 32 mmol) at room temperature for 2 days. The mixture was diluted with water then extracted with ether. The extract was dried ($MgSO_4$), the solvent was removed under vacuum, and the residue was purified by chromatography (silica gel) to give the title compound (1.94 g). MS (M+H), 263.

Step 278c. 4-amino-5-cyclohexyl-7-(4-(dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c first substituting 1,1-dicyano-3-cyclohexylethene (prepared according to the method of Moison, *et al.* (Tetrahedron (**1987**), 43:537-542) by treating cyclohexane carboxaldehyde with malononitrile in the presence of finely powdered magnesium oxide in dichloromethane) for the R3 reagent of Example 244 Step c, and substituting the compound from Step 278b for the R^4 reagent of Example 244 Step c, and also performing the condensation with ammonium acetate but also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 447; IR(cm-1) 3400, 2900, 1690, 1610, 1590, 1395.

Example 279

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine

Step 279a. 1-(5-methyethyl-2-pyridyl)ethanone

A solution of 2-acetyl-5-bromopyridine (1.45 g, 7.9 mmol), 2-propenyltrimethyltin (1.77 g, 8.7 mmol), $Pd_2(dba)_3$ (0.33 g, 0.36 mmol), and tri-2-furylphosphine (0.17 g, 0.72 mmol) in 25 mL of benzene was warmed at 60 °C for 4 hours. The reaction mixture was concentrated and the coupled product was purified by flash chromatography (1.22 g, 96 %). The product was dissolved in 25 mL of EtOH and the solution was purged with a stream of H_2. 10% Palladium on charcoal (50 mg) in 0.5 mL of EtOH was added and the reaction mixture was stirred for 12 h under an atmoshpere of H_2. The reaction mixture was filtered and the resulting solution was concentrated under reduced pressure. The title compound, **2**, (1.04 g, 84%) was isolated following flash chromatography.

Step 279b. 4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c substituting the compound from Step 279a for the R^4 reagent of Example 244 Step c, and performing the condensation with ammonium acetate and also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 421 (1Br); IR (cm-1) 3489, 2940, 1545, 1482, 1357.

Examples 280-281

Following the procedures of Example 244 Step c, except in step c substituting the compound shown below for the R^4 reagent of Example 244 Step c, and performing the

condensation with ammonium acetate and also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds shown in the table below were prepared.

Ex. No.	Name	R^4 Reagent (for 7-position)	Analytical Data
280	4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine	1-(5-piperidinyl-2-pyridyl)ethanone *	MS (M+H), 460 (1Br); IR (cm-1) 3064, 2937, 1556, 1493, 1358
281	4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine	1-(2-morpholinyl-5-pyridyl)ethanone **	MS (M+H), 491 (1 Br); IR (cm-1) 1585, 1555, 1505, 1240, 1110, 940

* Prepared as in Ex. 252b, except substituting morpholine for the bis(2-methoxyethyl)amine thereof.
** prepared by treatment of 5-acetyl-2-chloro-pyridine with morpholine in refluxing ethanol.

Example 282

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine

Step 282a. 4-cyanoacetophenone, acetal with 2,2-dimethylpropylene glycol

A sample of 4-cyanoacetophenone (4.35 g, 30 mmol) was dissolved in 150 mL of hexanes, and to this solution were added 2,2-dimethylpropylene glycol (3.44 g, 33 mmol) and a catalytic amount (10 mg) of p-toluene sulfonic acid. The reaction was heated overnight at reflux with a Dean-Stark trap, and an additional portion of glycol (33 mmol) was added. The reaction was continued for 3 hours, then cooled and the solvent was removed. The residue was dissolved in ethyl acetate, and this solution was washed with aqueous NaHCO3, water and brine, and dried over MgSO4. The solvent was removed under vacuum to give the title compound (7.46 g).

Step 282b. 4-(aminomethyl)acetophenone, acetal with 2,2-dimethylpropylene glycol

The compound from Step 282a (2.31 g, 10 mmol) was dissolved in ether (50 mL) and stirred with lithium aluminum hydride (0.76 g, 20 mmol) at ambient temperature overnight. The reaction was quenched with MgSO4•10 H2O, and the mixture was diluted with ether. The mixture was filtered, and the filtrate removed to give the title compound.

Step 282c. 1-(4-(BOC-aminomethyl)phenyl)ethanone

The compound from Step 282b (1.18 g, 5 mmol) was dissolved in THF (20 mL), 1N HCl (20 mL) was added, and the mixture was stirred for 2 days. The volatiles were removed under vacuum, the residue was dissolved in THF (20 mL), and d-tibutyl dicarbonate (2.18 g, 10 mmol) was added. The mixture was stirred at room temperature over a weekend. The solution was diluted with water, and the mixture was extracted with ether and ethyl acetate. The organic extracts were dired (MgSO4), and the solvent was remove under vacuum to give the title compound.

Step 282d. 4-amino-5-(3-bromophenyl)-7-(4-(N-formylamino)methyl)phenyl)pyrido[2,3-dlpyrimidine

Following the procedures of Example 244, except in step c substituting the compound from Step 282c for the R^4 reagent of Example 244 Step c, and performing the condensation with ammonium acetate but also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H) 434 (1 Br); IR (cm-1) 3440, 2700-3150, 1635, 1580, 1380.

Example 283

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-methylamino)-1-methylethyl)phenyl)pyrido[2,3-dlpyrimidine

Step 283a. 4-(1-amino-1-methylethyl)acetophenone

$CeCl_3$ (10 g, 34.9 mmol) was suspended in THF (60 mL), and the mixture was cooled to -78 °C. Methyl lithium (1.4 M, 2 mL) was added, and the mixture was stirred for 20 minutes. Then the compound from Example 282 Step a, (4-cyanoacetophenone acetal with 2,2-dimethylpropylene glycol, 2.31 g, 10 mmol) in 2 mL of THF was added. After stirring for 4 hours, the mixture was allowed to warm to room temperature while stirring for 16 hours. The reaction was quenched with water and ammonium hydroxide, filtered, and the filtrate was extracted with dichloromethane. The solution was dried ($MgSO_4$), and the solvent was removed to give the title compound.

Step 283b. 4-(1-(N-BOC-amino)-1-methylethyl)acetophenone

The compound from Step 283a (2.32 g, 8.77 mmol) was treated sequentially with HCl and di-t-butyl dicarbonate according to the procedure of Example 282 Step c to give the title compound (1.60 g). MS (M+H) 278.

Step 283c. 4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 244 Step c, except in step c substituting the compound from Step 283b for the R^4 reagent of Example 244 Step c, and performing the condensation with ammonium acetate but also substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the title compound was prepared. MS (M+H)
462 (1 Br); IR (cm-1) 3440, 1640, 1605, 1580, 1380.

Example 284

4-amino-5-(3-bromophenyl)-7-(4-(1-(N,N-dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine

Step 284a. 4-(1-(dimethylamino)-1-methylethyl)acetophenone

The compound from Step 283a (1.18 g, 5 mmol) was dissolved in 5 mL formic acid, and 5 mL of formalin (37%) was added. The mixture was heated at reflux for 4 hours, then cooled and neutralized with 2N Na_3CO_3. The mixture was extracted with dichloromethane. The solution was dried ($MgSO_4$), and the solvent was removed to give the title compound (0.94 g). MS (M+H) 462 (1 Br); IR (cm-1) 3520, 1640, 1610, 1580, 1375.

Examples 285-286

Following the procedures of Example 157, except substituting the appropriate reagents for the R^3 and R^4 reagents of Example 157 as indicated in the Table below, compounds of Examples 285-286 were prepared. For Example 286, treatment with aqueous HCl was omitted, and the free base was obtained.

Examples 285-286

Ex. No.	Name	R^3 Reagent (for 5-position	R^4 Reagent (for 7-position)	Analytical Data
285	4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(3-bromophenyl)propene	1-(N-acetyl-5-indolinyl)-ethanone	mp (hydrochloride salt) >270°C. IR (cm^{-1}) 3445, 3100-2500, 1640, 1605, 1445, 1395, 1325. LRMS $[M+H]^+$ m/z 460, 462.

286	4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-chloro-3-pyridyl)-ethanone	mp 240-242 °C. IR (cm-1) 3528, 3300, 3086, 2936, 2853, 1645, 1590, 1575, 1565,1350. LRMS [M+H]+ m/z 340.

Examples 287-300

Following the procedures of Example 157, except substituting the appropriate R^3 and R^4 reagents as indicated in the Table below and replacing the formamide or formamidine acetate treatment with treatment with triethyl orthoformate at reflux in the presence of a catalytic amount of ammonium sulfate, followed by cooling to 25 °C and addition of excess ammonia in ethanol, compounds of Examples 287-300 were prepared. . After 24 hours, the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichloroethane at reflux for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary. The treatment with aqueous HCl was omitted in some cases, and the free bases were obtained.

Examples 287-300

Ex. No.	Name	R^3 Reagent (for 5-position	R^4 Reagent (for 7-position)	Analytical Data
287	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-2-methyl-(3-(2-bromophenyl)propene	1-(6-dimethylamino-3-pyridyl)-ethanone	IR (cm-1) 2600-3500, 1650, 1602, 1596, 1520 cm-1. LRMS [M+H]+ m/z 449,451.
288	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-2-methyl-(3-(2-bromophenyl)propene	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 213-216 °C. IR (cm-1) 2400-3500, 1660, 1600. LRMS [M+H]+ m/z 491& 493.
289	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-(N-methyl-N-formyl)amino)-3-phenyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-2-methyl-(3-(2-bromophenyl)propene	1-(6-(N-methyl-N-formyl)amino)-3-pyridyl)-ethanone	mp 252-253°C. IR (cm^{-1}) 3515, 3310, 3200-2800, 1675, 1585, 1560, 1545, 1340. LRMS [M+H]+ m/z 462, 464.
290	4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 208-210. IR (cm-1) 3490, 3300, 3050-3250, 1620, 1580, 1550, 1490. LRMS [M+H]+ m/z 391.

291	4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(2-bromophenyl)propene	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 201-204 °C. IR (cm-1) 3601, 3500, 3310, 2960, 2850, 1585, 1561, 1502, 1345 . LRMS [M+H]+ m/z 477, 479.
292	4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-(4-tetrahydropyranyl)ethene *	1-(6-morpholinyl-3-pyridyl)-ethanone	mp (dihydrochloride salt) 213-216 °C. IR (cm-1) 3310, 3060, 2955, 1587, 1559, 1506, 1350. LRMS [M+H]+ m/z 393.
293	4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-dimethylamino-3-pyridyl)-ethanone	mp (dihydrochloride salt) 272-274 °C. IR (cm-1) 3532, 3294, 3100, 2930, 2853, 1606, 1586, 1560, 1522, 1387. LRMS [M+H]+ m/z 349.
294	4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-ethylpentene	1-(6-dimethylamino-3-pyridyl)-ethanone	mp (free base): 223.5-225 °C. IR (cm-1) 3480, 3000-3470, 2800-3000, 1630, 1610, 1580, 1565, 1520. LRMS [M+H]+ m/z 337.
295	4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclopentylethene	1-(6-morpholinyl-3-pyridyl)-ethanone	IR (cm^{-1}) 3495, 3320, 3080, 2950, 1645, 1600, 1500, 1400, 1350, 1240. LRMS $[M+H]^+$ m/z 377.
296	4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(2-chloro-3-pyridyl)-ethanone	IR (cm^{-1}) 3305, 3155, 2930, 2855, 1590, 1610, 1590, 1545, 1345. LRMS $[M+H]^+$ m/z 340, 342.
297	4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-(3,5-dimethylcyclohexyl)ethene	1-(6-dimethylamino-3-pyridyl)-ethanone	IR (cm^{-1}) 3310, 3100, 2950, 1605, 1590, 1555, 1390, 1350. LRMS $[M+H]^+$ m/z 377.
298	4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(4-(benzyloxycarbonyl)piperidin-1-yl)propene	1-(6-morpholinyl-3-pyridyl)-ethanone	IR (cm-1) 3538, 3311, 3032, 2925, 2852, 1696, 1585, 1560. LRMS [M+H]+ m/z 540.
299	4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(6-bromo-3-pyridyl)-ethanone	m.p. 250-252 °C, IR (cm-1) 3530, 3298, 3093, 2932, 2856, 1645, 1583, 1569, 1543, 1461, 1346. LRMS [M+H]+ 384, 386.
300	4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-3-cyclohexylethene	1-(3-cyanophenyl)-ethanone	m. p. 223-224 °C. IR (cm-1) 3528, 3298, 3075, 2937, 2235, 1645, 1586, 1548, 1567, 1463. LRMS [M+H]+ 332.

* The 1,1-dicyano-3-cyclohexylethene was prepared according to the method of Moison, *et al.* (Tetrahedron (**1987**), 43:537-542) by treating cyclohexane carboxaldehyde with malononitrile in the presence of finely powdered magnesium oxide in dichloromethane.

The reagents for the following examples were prepared by this method susbstituting the compound shown below for the cyclohexane carboxaldehyde used to prepare the reagent of Example 290.

Example 292, tetrahydropyran-4-carboxaldehyde;

Example 294, 2-ethylbutanaldehyde;

Example 295, cyclopentane carboxaldehyde;

Example 297, 3,5-dimethylcyclohexane carboxaldehyde;

Example 298, N-(phenylmethoxylcarbony)piperidine-4-carboxaldehyde (this material was prepared from N-(carbobenzyloxy)-4-(2-hydroxyethyl)piperidine (Brehm et al., Helv.Chim.Acta, 70; (**1987**), 1981-1987 by treatment with TEMPO (2,2,6,6-tetramethylpiperidinyloxy radical) and potassium bromide in dichloromethane at 0 °C to which was added commercial bleach (Clorox) containing sodium bicarbonate).

Examples 301-305

Following the procedures of Example 246, except in step (c) substituting the appropriate reagents for methylamine as indicated in the Table below to prepare the correct R^4 reagent, and substituting the R^3 reagent shown below for the R^3 reagent of Example 246 step d, the compounds of Examples 301-305 were prepared. For Example 302 only, the condensation solvent was DMSO instead of ethanol and dimethoxyethane.

Examples 301-305

Ex. No.	Name	R^3 reagent	reagent of step c	Analytical Data
301	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(2-bromophenyl)propene	dimethylamine	mp (dihydrochloride salt) >220°C. IR (cm^{-1}) 3500-2400, 1640, 1610, 1580, 1370. LRMS $[M+H]^+$ m/z 450, 452.
302	4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-(3-bromostyrene	imidazole sodium salt	mp (tetrahydrochloride salt) >240°C. IR (cm^{-1}) 3600-2400, 1640, 1610, 1590, 1560, 1415, 1370. LRMS $[M+H]^+$ m/z 445, 447.
303	4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-(3-bromostyrene	azacycloheptane	mp (dihydrochloride salt) >190°C. IR (cm^{-1}) 3435, 3100-2400, 1635, 1610, 1590, 1550, 1440, 1370. LRMS $[M+H]^+$ m/z 476, 478.
304	4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-(3-bromostyrene	N-methyl-N-(1-methylethyl))amine	mp (dihydrochloride salt) >210°C. IR (cm^{-1}) 3435, 3100-2400, 1635, 1610, 1590, 1550, 1410, 1370. LRMS $[M+H]^+$ m/z 450, 452.

305	4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine	1,1-dicyano-(3-(2-bromophenyl)propene	morpholine	IR (cm-1) 3475, 3313, 3100, 1650, 1620, 1580, 1555. LRMS [M+H]+ at 492, 494.

Example 306

4-amino-5-cyclohexyl-7-(6-(4-acetylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

A mixture of 679 mg (2 mmol) of the compound from Example 298 and 1.28 g (10 mmol) of N-acetylpiperazine in 5 mL of DMSO was heated at 110 °C for 5 hours. On cooling a precipitate was deposited, which was collected and washed with 20% methanol and dried to give 647 mg of the product as orange flakes: IR (cm-1) 3522, 3306, 3110, 2925, 2854, 1670, 1650, 1586, 1506. LRMS [M+H]+ m/z 432.

Examples 307-322

Follwing the procedure of Example 306, except substituting the reagent shown in the table below for the N-acetylpiperazine of Example 306, the compounds shown in the table were prepared. The compounds were purified by HPLC chromatography.

Ex. No.	Name	reagent	Analytical Data
307	4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	1-acetyl-1,4-diazacycloheptane	m.p. 169-171 °C. IR (cm-1) 3535, 3309, 3096, 2930, 2854, 1638, 1605, 1587, 1558, 1513. LRMS [M+H]+ 446.
308	4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	1-methyl-1,4-diazacycloheptane	LRMS $[M+H]^+$ 419.
309	4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine	N-methyl-N-(2-(2-pyridyl)ethyl)amine	LRMS $[M+H]^+$ 441.

3101	4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine	N,N-dimethyl, N'-methyl-1,2-ethylenediamine	LRMS $[M+H]^+$ 421.
311	4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	azetidine	LRMS $[M+H]^+$ 361.
312	4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine	N-methyl-N-(3-pyrrolidinyl)acetamide	LRMS $[M+H]^+$ 447.
313	4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine	pyrrolidine-2-formamide	LRMS $[M+H]^+$ 419.
314	4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl)pyrido[2,3-d]pyrimidine	1-phenyl-1,38-triazaspiro[4.5]decan-4-one	LRMS $[M+H]^+$ 536.
315	4-amino-5-cyclohexyl-7-(6-(2-(methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine	2-(methoxymethyl)pyrrolidine	LRMS $[M+H]^+$ 420.
316	4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine	N-(methoxyethyl)propylamine	LRMS $[M+H]^+$ 421.
317	4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine	2-(methylamino)-dimethylacetaldehyde	LRMS $[M+H]^+$ 429.
318	4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine	N-(4-piperidyl)-dimethylamine	LRMS $[M+H]^+$ 433.

319	4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine	piperidine-4-formamide	LRMS $[M+H]^+$ 433.
320	4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine	N^1, N^1-diethyl-N^3-methyl-1,3-propanediamine	LRMS $[M+H]^+$ 449.
321	4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine	N-methyl-(4-pyridyl)ethylamine	LRMS $[M+H]^+$ 441.
322	4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethyl)amino)pyrid-3-yl)pyrido[2,3-d]pyrimidine	N-methyl-(3-pyridyl)methylamine	LRMS $[M+H]^+$ 427.

Example 323

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine

The procedures of Example 157 were followed, except substituting 1',1'-dicyano-3-bromostyrene for the R^3 reagent and 1-(1-methyl-5-indolyl)-ethanone for the R^4 reagent. After 24 hours, the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichloroethane at reflux for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary. The treatment with aqueous HCl was omitted, and the free bases was obtained. IR (KBr) cm^{-1} 3500, 1578, 1500; MS *m/z* 431 $(M+H)^+$.

Example 324

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 323 by oxidation with CrO3 in sulfuric acid. IR (microscope) 3471, 1765, 1500 cm^{-1}; MS *m/z* 461$(M+H)^+$.

Examples 325-326

Following the procedures of Example 157, except substituting the appropriate R^3 and R^4 reagents as indicated in the Table below, compounds of Examples 325-326 were prepared. After 24 hours, the precipitated amidine compound was filtered and washed with hexanes, then dried under vacuum. The amidine compound was then heated in 1,2-dichloroethane at reflux for 1-8 hours. The reaction mixture was cooled to room temperature and purified by chromatography, and the product was recrystallized if necessary. The treatment with aqueous HCl was omitted in some cases, and the free bases were obtained.

Examples 325-326

Ex. No.	Name	R^3 Reagent (for 5-position	R^4 Reagent (for 7-position)	Analytical Data
325	4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-3-bromostyrene	1-(3-fluoro-4-(1-morpholinyl)phenyl)-ethanone	IR (microscope) 3443, 3044, 1639, 1606, 1584, 1520, 1362, 1245 cm^{-1}; MS *m/z* 480 $(M+H)^+$.
326	4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine	1',1'-dicyano-3-bromostyrene	1-(4-hydroxy-3-nitrophenyl)-ethanone	IR (KBr) 3461, 1623, 1579, 1548, 1523, 1353 cm^{-1}; MS *m/z* 438 $(M+H)^+$.

Example 327

Following the procedures of Example 244 Step c, except in step c substituting the compound resulting from the reaction of 2-acetyl-5-chloropyridine in refluxing ethanol with the precursor reagent compound (4-piperidinone ethylene ketal) shown below for the R^4 reagent of Example 244 Step c, and substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compound shown in the table below was prepared.

Ex. No.	Name	precursor reagent	Analytical Data
327	4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	4-piperidinone ethylene ketal	IR (microscope) 3091, 1602, 1580, 1558, 1512, 1353, 1236, 1103 cm^{-1}; MS *m/z* 519 $(M+H)^+$.

Example 328

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Treating the compound of Example 327 with dilute HCl, the title compound was prepared. IR (microscope) 3438, 3051, 1645, 1605, 1558, 1450, 1371, 1240 cm^{-1}; MS *m/z* 475 $(M+H)^+$.

Examples 329-331

Following the procedures of Example 244 Step c, except in step c substituting the compound resulting from the reaction of 2-acetyl-5-chloropyridine in refluxing ethanol with the precursor reagent compound shown below for the R^4 reagent of Example 244 Step c, and substituting dichloroethane as the solvent in place of the ethanol solvent in Example 244 step c, the compounds shown in the table below were prepared.

Examples 329-331

Ex. No.	Name	precursor reagent	Analytical Data
329	4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	piperazine	IR (KBr) 3489, 1674, 1602, 1581, 1559, 1503, 1233, 1004 cm^{-1}; MS *m/z* 491 $(M+H)^+$.
330	4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine	1-methylpiperazine	IR (microscope) 3438, 3051, 1540 cm^{-1}; MS *m/z* 477 $(M+H)^+$.
331	4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin	thiomorpholine	IR (KBr) 3486, 1602, 1581, 1560, 1502, 1228 cm^{-1}; MS *m/z* 479 $(M+H)^+$.

Example 332

4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The compound of Example 331 was treated with 4-chloroperbenzoic acid in methanol and dichloromethane to give the title compound. IR (microscope) 3471, 1601, 1581, 1562, 1510, 1353, 1316, 1285, 1122 cm^{-1}; MS *m/z* 511$(M+H)^+$.

Example 333

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Step 333a. 1',1'-dicyano-2-bromostyrene

The title compound was prepared by condensation of 2-bromobenzaldehyde with malononitrile and MgO in dichloromethane by the standard procedure of Broekhuis et al. (*Recl. J. R. Neth. Chem. Soc.*, 99: 6-12 (**1980**)).

Step 333b. 5-acetyl-2-morpholinylpyridine

The title compound was prepared by the reaction of 5-acetyl-2-chloropyridine with morpholine in refluxing ethanol.

Step 333c. 4-(2-bromophenyl)-3-cyano-6-morpholinylpyridine-2-amine

The title compound was prepared by condensation of 1',1'-dicyano-2-bromostyrene with 5-acetyl-2-morpholinylpyridine and ammonium acetate in dichloroethane at reflux. After the reaction was complete (TLC), the mixture was cooled, and the solvent was removed. The residue was triturated with methanol to give the product.

Step 333d. 4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

A sample of 4-(2-bromophenyl)-3-cyano-6-morpholinylpyridine-2-amine was heated at 180-190 °C in formamide. The reaction was monitored by TLC, and when the reaction was complete the mixture was cooled to room temperature. The product was allowed to precipitate, then recovered by filtration and washed with water. Additional product was extracted from the filtrate. The product was purified by column chromatography eluting with 10% MeOH/CH_2Cl_2. IR (microscope) 3493, 1547, 1109cm^{-1}; MS *m/z* 464 $(M+H)^+$.

Examples 334-336

Following the procedures of Example 333, except in Step a substituting the precursor aldehyde reagent shown below for the 2-bromobenzaldehyde of Example 333 Step a, and carrying the product forward as in procedures 333 Stepbs b-d, the compounds shown in the table below were prepared.

Examples 334-336

Ex. No.	Name	precursor aldehyde reagent	Analytical Data
334	4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	3-bromo-4-methoxybenzaldehyde	IR (microscope) 3486, 1600, 1575, 1562, 1500, 1260, 1237 cm^{-1}; MS *m/z* 493 $(M+H)^+$.
335	4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	4-bromobenzaldehyde	IR (microscope) 3497, 1532, 1098cm^{-1}; MS *m/z* 464 $(M+H)^+$.
336	4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine	3-chlorobenzaldehyde	IR (microscope) 3484, 1500, 1034cm^{-1}; MS (FAB) *m/z* 587 $(M+H)^+$.

Example 337

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine

Following the procedures of Example 333, except in Step a substituting 3-bromobenzaldehyde for the 2-bromobenzaldehyd, in Step b substituting 5-acetyl-2,3-dichloropyridine for the 5-acetyl-2-chloropyridine to give 5-acetyl-3-chloro-2-morpholinylpyridine, and substituting 5-acetyl-3-chloro-2-morpholinylpyridine for the 5-acetyl-2-morpholinylpyridine in step c, then the carrying the product forward as in Example 333 Step d, the title compound was prepared. IR (microscope) 3493, 1635, 1585, 1555, 1492, 1340, 1241, 1113 cm^{-1}; MS *m/z* 497 $(M+H)^+$.

Example 338

4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared by treating the compound of Example 134 with hydrogen peroxide in acetic acid according to standard procedures. IR (microscope) 3486, 1579, 1552, 1353, 1121, 1020 cm^{-1}; MS *m/z* 479 $(M+H)^+$.

Example 339

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine

Step 339a. 1',1'-dicyano-3-bromostyrene

The title compound was prepared by condensation of 3-bromobenzaldehyde with malononitrile and MgO in dichloromethane by the standard procedure of Broekhuis et al. (*Recl. J. R. Neth. Chem. Soc.*, 99: 6-12 (**1980**)).

Step 339b. 5-acetyl-2-(N-(2-ethoxyethyl)amino)pyridine

The title compound was prepared by the reaction of 5-acetyl-2-chloropyridine with 2-ethoxyethylamine in refluxing ethanol.

Step 339c. 4-(3-bromophenyl)-3-cyano-6-(N-(2-ethoxyethyl)amino)pyridine-2-amine

The title compound was prepared by condensation of 1',1'-dicyano-2-bromostyrene with 5-acetyl-2-morpholinylpyridine and ammonium acetate in dichloroethane at reflux. After the reaction was complete (TLC), the mixture was cooled, and the solvent was removed. The residue was triturated with methanol to give the product.

Step 339d. 4-amino-5-(2-bromophenyl)-7-(6-(N-(2-ethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine

A sample of the compound from Step 239d was treated according to the procedure of Example 233d to give the title compound. IR (microscope) 3301, 1610, 1579, 1543, 1346, 1304, 1120 cm^{-1}; MS *m/z* 481 $(M+H)^+$.

Example 340

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine

This compound was isolated by chromatography as a product of the reaction described in Example 239 Step d. IR (microscope) 3306, 1679, 1596, 1577, 1548, 1493, 1352, 1125 cm^{-1}; MS *m/z* 509 $(M+H)^+$.

Example 341

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine

The title compound was prepared by treating the compound of Example 341 with hydrogen peroxide in acetic acid according to standard procedures. IR (microscope) 3296, 1628, 1560, 1411, 1353 cm^{-1}; MS *m/z* 497 $(M+H)^+$.

Example 342

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 328 by reduction with (Lithium Aluminum Hydride, and subsequent workup acccording to standard procedures). IR (microscope) 3349, 1510, 1116 cm^{-1}; MS *m/z* 478 $(M+H)^+$.

Example 343

1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt

The title compound was prepared from the compound of Example 342 by treatment with $POCl_3$, and subsequent workup acccording to standard procedures. IR (microscope) 3498, 1500, 1444 cm^{-1}; MS *m/z* 556 $(M+H)^+$.

Example 344

4-amino-5-(3-bromophenyl)-7-(6-(2-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 339 by oxidation of the free hydroxy group to an aldehyde with TEMPO reagent. During workup of the mixture, the compound self-condensed to give the title compound. IR (microscope) cm^{-1}; MS *m/z* 492 $(M+CH_3OH-H_2O)^+$.

Example 345

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 328 by treatment with methyl triphenylphosphine bromide at -78 °C in DMSO. After quenching and warming the mixture to room temperature, the title compound was extracted, then purified by chromatography. IR (microscope) 3055, 1602, 1559, 1508, 1440, 1344, 1174 cm^{-1}; MS *m/z* 473 $(M+H)^+$.

Example 346

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 345 by treatment with OsO_4 in DMSO at room temperature. After quenching, the title compound was extracted, then purified by chromatography. IR (microscope) 3304, 1603, 1580, 1557, 1509, 1352, 1241 cm^{-1}; MS *m/z* 507 $(M+H)^+$.

Example 347

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Step 347a. 1,1-dicyano-3-cyclohexylethene

The 1,1-dicyano-3-cyclohexylethene was prepared according to the method of Moison, *et al.* (Tetrahedron (**1987**), 43:537-542) by treating cyclohexane carboxaldehyde with malononitrile in the presence of finely powdered magnesium oxide in dichloromethane.

Step 347b. 2-acetyl-5-(4,4-ethylenedioxypiperidinyl)pyridine

A sample of 2-acetyl-5-chloropyridine was treated in refluxing ethanol with 4-piperidinone ethylene ketal to give the title compound.

Step 347c. 4-amino-5-cyclohexyl-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

Following the procedures of example 339 Step c, except substituting the compounds from Step 347a and 347b for the compounds of Steps 339a and 339b, and carrying the product forward according to the procedure of example 339 Step d, the title compound was prepared. IR (microscope) 2929, 1604, 1585, 1557, 1514, 1426, 1344, 1238, 1106 cm^{-1}; MS *m/z* 447 $(M+H)^+$.

Example 348

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 347 by treatment with dilute HCl in ethanol. The title compound was purified by chromatography. IR (microscope) 2928, 1715, 1603, 1585, 1559, 1507, 1344, 1226 cm^{-1}; MS *m/z* 403 $(M+H)^+$.

Example 349

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine

The title compound was prepared from the compound of Example 348 by treatment with methyl triphenylphosphine bromide at -78 °C in DMSO. After quenching and warming the mixture to room temperature, the title compound was extracted, then purified by chromatography. IR (microscope) 2929, 1604, 1584, 1557, 1506, 1342, 1239 cm^{-1}; MS *m/z* 401 $(M+H)^+$.

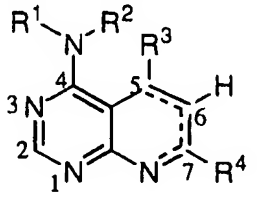
Example 350

4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine

This compound was isolated from the reaction mixture of Example 293 as a side product: IR (cm-1) 3289, 3089, 2930, 2841, 1674, 1606, 1559, 1531. LRMS [M+H]+ m/z 376.

WHAT IS CLAIMED IS:

1. A method for inhibiting adenosine kinase by administering a compound, or a pharmaceutically acceptable salt or amide thereof, having the formula



(I)

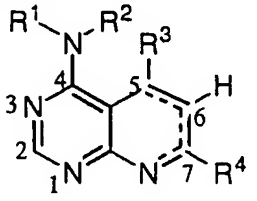
wherein

R^1 and R^2 are independently selected from H, loweralkyl, C_1-C_6alkoxyC_1-C_6alkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group, heteroarylalkyl or heterocycloalkyl wherein the heteroaryl and heterocyclic groups are linked directly or indirectly by a ring carbon;

R^4 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group heteroarylalkyl or heterocycloalkyl; and a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained, in vitro or to a mammal.

2. A method of inhibiting adenosine kinase according to Claim 1 comprising administering a compound of formula I



(I)

wherein

R^1 and R^2 are independently selected from H, loweralkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to from a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 and R^4 are independently selected from the group consisting of:

C_1-C_6alkyl,
C_2-C_6alkenyl,
C_2-C_6alkynyl,
C_3-C_8cycloalkyl,
heteroarylC_0-C_6alkyl or substituted heteroarylC_0-C_6alkyl,
optionally substituted cycloalkyl,
arylC_0-C_6alkyl or substituted arylC_0-C_6alkyl,
heteroarylC_2-C_6alkenyl or substituted heteroarylC_2-C_6alkenyl,
arylC_2-C_6alkenyl or substituted arylC_2-C_6alkenyl,
heteroarylC_2-C_6alkynyl or substituted heteroarylC_2-C_6alkynyl,
arylC_2-C_6alkynyl or substituted arylC_2-C_6alkynyl wherein the 1-4 heteroaryl or aryl substituents are independently selected from

halogen, oxo, CO_2R^5, cyanoC_1-C_6alkyl, heteroarylC_0-C_6alkyl, heterocyclicC_0-C_6alkyl, C_1-C_6alkyloxy, C_1-C_6alkyloxyC_1-C_6alkyl, arylC_0-C_6alkyl, arylC_1-C_6alkyloxy, $R^5R^6NC(O)$, cyano, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6alkyl, C_2-C_6alkenyldialkylmalonyl, CF_3, HO-, C_1-C_6alkyloxyC_1-C_6alkyloxy, C_1-C_6alkylSO_n wherein n is 1-2, C_1-C_6alkylthio, C_1-C_6alkylacryl, CF_3O, CF_3, C_1-C_4alkylenedioxy, C_1-C_6alkylacryl, $R^5R^6N(CO)NR^5$, N-formyl(heterocyclic), NO_2, $NR^5R^6C_0$-C_6alkyl, $(R^5O)(R^6O)$-P(O)-C_0-C_6alkyl,

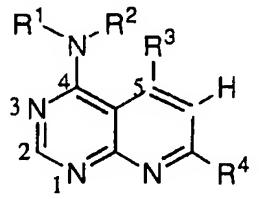
wherein R^5 and R^6 are independently selected from H, C_1-C_6alkyl, HC(O), C_1-C_6alkyloxyC_1-C_6alkyl, C_1-C_6alkyloxy, C_1-C_6alkylC(O), $CF_3C(O)$, $NR^7R^8C_1$-C_6alkyl, phthalimidoC_1-$C_6C(O)$, C_1-C_6alkylSO_n where n is 1-2, CNC_1-C_6alkyl, $R^7R^8NC(O)NR^7$-, heteroaryl, $NR^7R^8C_1$-C_6alkylC(O), C_1-C_6alkyloxycarbamidoC_1-C_6alkyl,

wherein R^7 and R^8 are independently selected from those variables identified for R^5 and R^6 or

R^5 and R^6 or R^7 and R^8 may join together with the nitrogen atom to which they are attached to form a 5-7 membered unsubstituted or substituted ring optionally containing 1-3 additional heteroatoms selected from O, N or S wherein the substituents are selected from C_1-C_6alkyl and

a dashed line --- indicates a double bond is optionally present.

3. A method according to Claim 2 wherein the method of inhibiting adenosine kinase comprises administering a pharmaceutically effective amount of a compound of formula II



(II)

wherein R^1-R^8 and n are as defined above to a patient in need of treatment thereof.

4. A method according to Claim 3 wherein R^4 is selected from the group consisting of: phenyl; thiophene-2-yl; 3-methyl-2-oxobenzoxazolin-6-yl; 2-(dimethylamino)-5-pyrimidinyl; 2-(N-formyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methylamino)5-pyrimidinyl; 2-(1-morpholinyl)-5-pyrimidinyl; 2-(1-pyrrolidinyl)-5-pyrimidinyl; 2-dimethylamino-5-pyrimidinyl; 2-furanyl; 2-oxobenzoxazolin-6-yl; 2-pyridyl; 3-(dimethylamino)phenyl; 3-amino-4-methoxyphenyl; 3-bromo-4-(dimethylamino)phenyl; 3-methoxyphenyl; 3-methyl-4-(N-acetyl-N-methylamino)phenyl; 3-methyl-4-(N-formyl-N-methylamino)phenyl; 3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl; 3-methyl-4-(N-methylamino)phenyl; 3-methyl-4-pyrrolidinylphenyl; 3-pyridyl; 3,4-dichlorophenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 4-(acetylamino)phenyl; 4-(dimethylamino)-3-fluorophenyl; 4-(dimethylamino)phenyl; 4-(imidazol-1-yl)phenyl; 4-(methylthio)phenyl; 4-(morpholinyl)phenyl; 4-(N-(2-(dimethylamino)ethyl)amino)phenyl; 4-(N-(2-methoxyethyl)amino)phenyl; 4-(N-acetyl-N-methylamino)phenyl; 4-(N-ethyl-N-formylamino)phenyl; 4-(N-ethylamino)phenyl; 4-(N-formyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-isopropylamino)phenyl; 4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl; 4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl; 4-(N-methyl-N-(2-cyano)ethylamino)phenyl; 4-(N-methyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-methyl-N-(3-methoxy)propionylamino)phenyl; 4-(N-methyl-N-acetylamino)phenyl; 4-(N-methyl-N-formylamino)phenyl; 4-(N-methyl-N-trifluoroacetylamino)phenyl; 4-(N-morpholinyl)phenyl; 4-(thiophene-2-yl)phenyl; 4-(ureido)phenyl; 4-(2-(dimethylamino)acetylamino)phenyl; 4-(2-methoxy)acetylamino)ethyl)amino)phenyl; 4-(2-methoxy)ethoxyphenyl; 4-(2-oxo-3-oxazolidinyl)phenyl; 4-(4-methoxy-2-butyl)phenyl; 4-(4-methylpiperidinyl)phenyl; 4-(5-pyrimidinyl)phenyl; 4-aminophenyl; 4-bromophenyl; 4-butoxyphenyl; 4-carboxamidophenyl; 4-chlorophenyl; 4-cyanophenyl; 4-diethylaminophenyl; 4-diethylmalonylallylphenyl; 4-dimethylaminophenyl; 4-

ethoxyphenyl; 4-ethylphenyl; 4-fluorophenyl; 4-hydroxyphenyl; 4-imidazolylphenyl; 4-iodophenyl; 4-isopropylphenyl; 4-methoxyphenyl; 4-methylaminophenyl; 4-methylsulfonylphenyl; 4-morpholinylphenyl; 4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl; 4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl; 4-N-ethyl-N-(2-methoxyethyl)amino)phenyl; 4-N-formylpiperazinylphenyl) 4-nitrophenyl; 4-piperidinylphenyl; 4-(3-pyridyl)phenyl; 4-pyrrolidinylphenyl; 4-t-butylacrylphenyl; 5-(dimethylamino)thiophene-2-yl; 5-amino-2-pyridyl; 5-dimethylamino-2-pyrazinyl; 3-dimethylaminopyridazin-6-yl; 5-dimethylamino-2-pyridyl; 5-pyrimidinylphenyl; 6-(N-methyl-N-formylamino)-3-pyridinyl; 6-(N-methyl-N-methoxyethylamino)-3-pyridinyl; 6-(2-oxo-3-oxazolidinyl)-3-pyridinyl; 6-dimethylamino-3-pyridinyl; 6-imidazolyl-3-pyridinyl; 6-morpholinyl-3-pyridinyl; 6-pyrrolidinyl-3-pyridinyl; 6-(2-propyl)-3-pyridinyl; and (4-formylamino)phenyl.

5. A method according to Claim 3 wherein R^3 is selected from the group consisting of (thiophene-2-yl)methyl; (thiophene-3-yl)methyl; butyl; cycloheptyl; pentyl; thiophene-2-yl; 1-(3-bromophenyl)ethyl; 2-(N-phenylmethoxycarbonyl)aminophenyl; 2-(3-bromophenyl)ethyl; 2-(3-cyanophenyl)methyl; 2-(4-bromophenyl)ethyl; 2-(5-chloro-2-(thiophen-3-yl)phenyl; 2-bromophenyl; 2-furanyl; 2-methylpropyl; 2-phenylethyl; phenylmethyl; 2,3-dimethoxyphenyl; 2,3-methylenedioxyphenyl; 3-(furan-2-yl)phenyl; 3-(thiophen-2-yl)phenyl; 3-(2-pyridyl)phenyl; 3-(3-methoxybenzyl)phenyl; 2-(3-aminopropynyl)phenylmethyl; 3-benzyloxyphenyl; 3-bromo-4-fluorophenyl; 3-bromo-5-iodophenyl; 3-bromo-5-methoxyphenyl; 3-bromophenyl; 3-bromophenyl)methyl; 3-carboxamidophenyl; 3-chlorophenyl; 3-cyanophenyl; 3-diethylmalonylallylphenyl; 3-dimethylaminophenyl; 3-ethoxyphenyl; 3-fluoro-5-trifluoromethylphenyl; 3-fluorophenyl; 3-hydroxyphenyl; 3-iodophenyl; 3-methoxyethyoxyphenyl; 3-methoxyphenyl; 3-methylphenyl; 3-methylsulfonylphenyl; 3-methylthiophenyl; 3-t-butylacrylphenyl; 3-trifloromethyoxyphenyl; 3-trifluoromethylphenyl; 3-vinylpyridinylphenyl; 3,4-dichlorophenyl; 3,4-dimethoxyphenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 3,5-di(trifluoromethyl)phenyl; 3,5-dibromophenyl; 3,5-dichlorophenyl; 3,5-dimethoxyphenyl; 3,5-dimethylphenyl; 4-(2-propyl)phenyl; 4-(2-propyl)oxyphenyl; 4-benzyloxyphenyl; 4-bromophenyl; 4-bromothiophene-2-yl; 4-butoxyphenyl; 4-dimethylaminophenyl; 4-fluoro-3-trifluoromethylphenyl; 4-methoxyphenyl; 4-neopentylphenyl; 4-phenoxyphenyl; 5-bromothiophene-2-yl; 5-cyclohexyl; 5-cyclopropyl; 5-hexyl; 5-methyl; 5-phenyl; (2-bromo-5-chlorophenyl)methyl; (2-bromophenyl)methyl; and (5-chloro-2-(3-methoxyphenyl)phenyl)methyl.

6. A method according to Claim 1 wherein the compound is selected from:

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacrylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-phenylpyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifloromethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methoxyethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;
4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl))-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine:

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

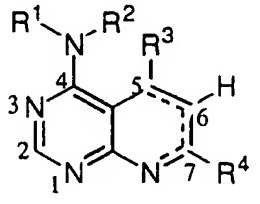
4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine.

7. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to Claim 1 in combination with a pharmaceutically acceptable carrier.

8. A method of treating ischemia, neurological disorders, nociperception , inflammation, immunosuppression, gastrointestinal disfunctions, diabetes and sepsis in a mammal in need of such treatment, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1 or 3.

9. A method according to Claim 8 wherein the method consists of treating cerebral ischemia, myocardial ischemia, angina, coronary artery bypass graft surgery, percutaneous transluminal angioplasty, stroke, thrombotic and embolic conditions, epilepsy, anxiety, schizophrenia, pain perception, neuropathic pain, visceral pain, arthritis, sepsis, diabetes and abnormal gastrointestinal motility.

10. A compound, or a pharmaceutically acceptable salt or amide thereof, of formula (I)



(I)

wherein

R^1 and R^2 are independently selected from H, loweralkyl, C_1-C_6alkoxyC_1-C_6alkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to form a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group, heteroarylalkyl or heterocycloalkyl wherein the heteroaryl and heterocyclic groups are linked directly or indirectly by a ring carbon;

R^4 is selected from the group consisting of loweralkyl, loweralkenyl, loweralkynyl, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclic group heteroarylalkyl or heterocycloalkyl; and a dashed line --- indicates that a double bond is optionally present provided that proper valencies are maintained;

with the proviso that the compound may not be selected from the group consisting of:

(a) 4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

(b) 4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

(c) 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

(d) 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

(e) 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

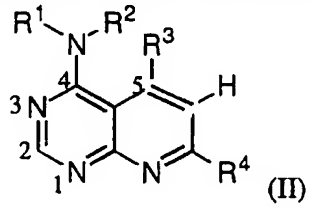
(f) 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

(g) 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

(h) 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine; and

(i) 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

11. A compound according to Claim 10 of formula II



(II)

wherein

R^1 and R^2 are independently selected from H, loweralkyl, arylC_1-C_6alkyl, -C(O)C_1-C_6alkyl, -C(O)aryl, -C(O)heterocyclic or may join together with the nitrogen to which they are attached to from a 5-7 membered ring optionally containing 1-2 additional heteroatoms selected from O, N or S;

R^3 and R^4 are independently selected from the group consisting of:

C_1-C_6alkyl,

C_2-C_6alkenyl,
C_2-C_6alkynyl,
C_3-C_8cycloalkyl,
heteroarylC_0-C_6alkyl or substituted heteroarylC_0-C_6alkyl,
optionally substituted cycloalkyl,
arylC_0-C_6alkyl or substituted arylC_0-C_6alkyl,
heteroarylC_2-C_6alkenyl or substituted heteroarylC_2-C_6alkenyl,
arylC_2-C_6alkenyl or substituted arylC_2-C_6alkenyl,
heteroarylC_2-C_6alkynyl or substituted heteroarylC_2-C_6alkynyl,
arylC_2-C_6alkynyl or substituted arylC_2-C_6alkynyl wherein the 1-4 heteroaryl or aryl substituents are independently selected from
halogen, oxo, CO_2R^5, cyanoC_1-C_6alkyl, heteroarylC_0-C_6alkyl, heterocyclicC_0-C_6alkyl, C_1-C_6alkyloxy, C_1-C_6alkyloxyC_1-C_6alkyl, arylC_0-C_6alkyl, arylC_1-C_6alkyloxy, $R^5R^6NC(O)$, cyano, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6alkyl, C_2-C_6alkenyldialkylmalonyl, CF_3, HO-, C_1-C_6alkyloxyC_1-C_6alkyloxy, C_1-C_6alkylSO_n wherein n is 1-2, C_1-C_6alkylthio, C_1-C_6alkylacryl, CF_3O, CF_3, C_1-C_4alkylenedioxy, C_1-C_6alkylacryl, $R^5R^6N(CO)NR^5$, N-formyl(heterocyclic), NO_2, $NR^5R^6C_0$-C_6alkyl, $(R^5O)(R^6O)$-P(O)- C_0-C_6alkyl,
wherein R^5 and R^6 are independently selected from H, C_1-C_6alkyl, HC(O), C_1-C_6alkyloxyC_1-C_6alkyl, C_1-C_6alkyloxy, C_1-C_6alkylC(O), $CF_3C(O)$, $NR^7R^8C_1$-C_6alkyl, phthalimidoC_1-$C_6C(O)$, C_1-C_6alkylSO_n where n is 1-2, CNC_1-C_6alkyl, $R^7R^8NC(O)NR^7$-, heteroaryl, $NR^7R^8C_1$-C_6alkylC(O), C_1-C_6alkyloxycarbamidoC_1-C_6alkyl,
wherein R^7 and R^8 are independently selected from those variables identified for R^5 and R^6 or
R^5 and R^6 or R^7 and R^8 may join together with the nitrogen atom to which they are attached to form a 5-7 membered unsubstituted or substituted ring optionally containing 1-3 additional heteroatoms selected from O, N or S wherein the substituents are selected from C_1-C_6alkyl and

with the proviso that the compound may not be selected from the group consisting of:

(a) 4-amino-5-(4-chlorophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
(b) 4-amino-5-(4-methoxyphenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;
(c) 4-amino-5-(4-fluorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;
(d) 4-amino-5-(4-chlorophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;

(e) 4-amino-5-phenyl-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

(f) 4-amino-5-phenyl-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

(g) 4-amino-5-(4-methoxyphenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

(h) 4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine; and

(i) 4-amino-5,7-diphenylpyrido[2,3-d]pyrimidine.

12. A compound according to Claim 10, wherein R^4 is selected from the group consisting of: phenyl; thiophene-2-yl; 3-methyl-2-oxobenzoxazolin-6-yl; 2-(dimethylamino)-5-pyrimidinyl; 2-(N-formyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl; 2-(N-methylamino)5-pyrimidinyl; 2-(1-morpholinyl)-5-pyrimidinyl; 2-(1-pyrrolidinyl)-5-pyrimidinyl; 2-dimethylamino-5-pyrimidinyl; 2-furanyl; 2-oxobenzoxazolin-6-yl; 2-pyridyl; 3-(dimethylamino)phenyl; 3-amino-4-methoxyphenyl; 3-bromo-4-(dimethylamino)phenyl; 3-methoxyphenyl; 3-methyl-4-(N-acetyl-N-methylamino)phenyl; 3-methyl-4-(N-formyl-N-methylamino)phenyl; 3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl; 3-methyl-4-(N-methylamino)phenyl; 3-methyl-4-pyrrolidinylphenyl; 3-pyridyl; 3,4-dichlorophenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 4-(acetylamino)phenyl; 4-(dimethylamino)-3-fluorophenyl; 4-(dimethylamino)phenyl; 4-(imidazol-1-yl)phenyl; 4-(methylthio)phenyl; 4-(morpholinyl)phenyl; 4-(N-(2-(dimethylamino)ethyl)amino)phenyl; 4-(N-(2-methoxyethyl)amino)phenyl; 4-(N-acetyl-N-methylamino)phenyl; 4-(N-ethyl-N-formylamino)phenyl; 4-(N-ethylamino)phenyl; 4-(N-formyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-isopropylamino)phenyl; 4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl; 4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl; 4-(N-methyl-N-(2-cyano)ethylamino)phenyl; 4-(N-methyl-N-(2-methoxyethyl)amino)phenyl; 4-(N-methyl-N-(3-methoxy)propionylamino)phenyl; 4-(N-methyl-N-acetylamino)phenyl; 4-(N-methyl-N-formylamino)phenyl; 4-(N-methyl-N-trifluoroacetylamino)phenyl; 4-(N-morpholinyl)phenyl; 4-(thiophene-2-yl)phenyl; 4-(ureido)phenyl; 4-(2-(dimethylamino)acetylamino)phenyl; 4-(2-methoxy)acetylamino)ethyl)amino)phenyl; 4-(2-methoxy)ethoxyphenyl; 4-(2-oxo-3-oxazolidinyl)phenyl; 4-(4-methoxy-2-butyl)phenyl; 4-(4-methylpiperidinyl)phenyl; 4-(5-pyrimidinyl)phenyl; 4-aminophenyl; 4-bromophenyl) 4-butoxyphenyl; 4-carboxamidophenyl; 4-chlorophenyl; 4-cyanophenyl; 4-diethylaminophenyl; 4-diethylmalonylallylphenyl) 4-dimethylaminophenyl) 4-ethoxyphenyl; 4-ethylphenyl; 4-fluorophenyl; 4-hydroxyphenyl; 4-imidazolylphenyl; 4-iodophenyl; 4-isopropylphenyl; 4-methoxyphenyl) 4-methylaminophenyl; 4-methylsulfonylphenyl; 4-morpholinylphenyl; 4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl; 4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl; 4-N-ethyl-N-

(2-methoxyethyl)amino)phenyl; 4-N-formylpiperazinylphenyl) 4-nitrophenyl; 4-piperidinylphenyl; 4-(3-pyridyl)phenyl; 4-pyrrolidinylphenyl; 4-t-butylacrylphenyl; 5-(dimethylamino)thiophene-2-yl; 5-amino-2-pyridyl; 5-dimethylamino-2-pyrazinyl; 5-dimethylamino-2-pyridyl; 5-pyrimidinylphenyl; 6-(N-methyl-N-formylamino)-3-pyridinyl; 6-(N-methyl-N-methoxyethylamino)-3-pyridinyl; 6-(2-oxo-3-oxazolidinyl)-3-pyridinyl; 6-dimethylamino-3-pyridinyl; 6-imidazolyl-3-pyridinyl; 6-morpholinyl-3-pyridinyl; 6-pyrrolidinyl-3-pyridinyl; 6-(2-propyl)-3-pyridinyl; and (4-formylamino)phenyl.

13. A compound according to Claim 10, wherein R^3 is selected from the group consisting of: (thiophene-2-yl)methyl; (thiophene-3-yl)methyl; butyl; cycloheptyl; pentyl; thiophene-2-yl; 1-(3-bromophenyl)ethyl; 2-(N-phenylmethoxycarbonyl)aminophenyl; 2-(3-bromophenyl)ethyl; 2-(3-cyanophenyl)methyl; 2-(4-bromophenyl)ethyl; 2-(5-chloro-2-(thiophen-3-yl)phenyl; 2-bromophenyl; 2-furanyl; 2-methylpropyl; 2-phenylethyl; phenylmethyl; 2,3-dimethoxyphenyl; 2,3-methylenedioxyphenyl; 3-(furan-2-yl)phenyl; 3-(thiophen-2-yl)phenyl; 3-(2-pyridyl)phenyl; 3-(3-methoxybenzyl)phenyl; 2-(3-aminopropynyl)phenylmethyl; 3-benzyloxyphenyl; 3-bromo-4-fluorophenyl; 3-bromo-5-iodophenyl; 3-bromo-5-methoxyphenyl; 3-bromophenyl; 3-bromophenyl)methyl; 3-carboxamidophenyl; 3-chlorophenyl; 3-cyanophenyl; 3-diethylmalonylallylphenyl; 3-dimethylaminophenyl; 3-ethoxyphenyl; 3-fluoro-5-trifluoromethylphenyl; 3-fluorophenyl; 3-hydroxyphenyl; 3-iodophenyl; 3-methoxyethyoxyphenyl; 3-methoxyphenyl; 3-methylphenyl; 3-methylsulfonylphenyl; 3-methylthiophenyl; 3-t-butylacrylphenyl; 3-trifloromethyoxyphenyl; 3-trifluoromethylphenyl; 3-vinylpyridinylphenyl; 3,4-dichlorophenyl; 3,4-dimethoxyphenyl; 3,4-methylenedioxyphenyl; 3,4,5-trimethoxyphenyl; 3,5-di(trifluoromethyl)phenyl; 3,5-dibromophenyl; 3,5-dichlorophenyl; 3,5-dimethoxyphenyl; 3,5-dimethylphenyl; 4-(2-propyl)phenyl; 4-(2-propyl)oxyphenyl; 4-benzyloxyphenyl; 4-bromophenyl; 4-bromothiophene-2-yl; 4-butoxyphenyl; 4-dimethylaminophenyl; 4-fluoro-3-trifluoromethylphenyl; 4-methoxyphenyl; 4-neopentylphenyl; 4-phenoxyphenyl; 5-bromothiophene-2-yl; 5-cyclohexyl; 5-cyclopropyl; 5-hexyl; 5-methyl; 5-phenyl; (2-bromo-5-chlorophenyl)methyl; (2-bromophenyl)methyl; and (5-chloro-2-(3-methoxyphenyl)phenyl)methyl.

14. A compound according to Claim 10, or a pharmaceutically acceptable salt or amide thereof, which is

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-(2-propyl)phenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-neopentylphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-butyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2.3-d]pyrimidine;
4-amino-5-(4-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-(2-propyl)oxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-butoxyphenyl)-7-(4-N-formylpiperazinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-benzyloxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-phenoxyphenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-(2-propyl)phenyl)-7-(4-diethylmalonylallylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-(2-propyl)phenyl)-7-(4-t-butylacrylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,4-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-t-butylacrylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-methoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethoxyphenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-diethylmalonylallylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-vinylpyridinylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-carboxamidophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-cyanophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-benzyloxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-methoxyphenyl)-7-(4-methoxyphenyl)pyrido[2.3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-butoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-(2-pyridyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-methylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-chlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-methoxyphenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-phenylpyrido [2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-ethylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-cyanophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-hydroxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-iodophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-ethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-trifloromethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-hydroxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-(imidazol-1-yl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-chlorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-isopropylphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-trifluorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-(3-methoxybenzyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-methoxyethyoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,4-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-ethoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(2'-thiophene)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)-7-(4-fluorophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-dimethylaminophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,4,5-trimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-methylenedioxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(thiophen-2-yl)-7-(4-morpholinylphenyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(thiophen-2-yle)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxamidophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)ethoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-trifluoromethylphenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-aminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(thiophene-2-yl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(2-furanyl)pyrido [2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-imidazolylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(thiophene-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(4-(3-pyridyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-morpholinyl-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(5-bromothiophene-2-yl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethoxyphenyl)-7-(5-pyrimidinylphenyl)pyrido[2,3-d]pyrimidine;

4-(4-fluorophenyl)amino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(dimethylamino)thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-iodophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-di(trifluoromethyl)phenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromothiophene-2-yl)-7-(4-(4-methylpiperidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dibromophenyl)-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(methylthio)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3,4-dichlorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-amino-4-methoxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-trifluoroacetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylamino)-3-fluorophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethyl-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4,4-bis(acetylamino)-5-(3-bromophenyl)-7-(4-(N-methyl-N-acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-isopropylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-ethyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(3-methoxypropionyl)-N-isopropyl-amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-N-(2-(dimethylamino)ethyl)-N-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-(dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-cyano)ethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(3-methoxy)propionylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-formyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(4-methoxy-2-butyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-(N-phthalimidyl)acetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-methyl-N-(trifluoroacetyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-(N-acetyl-N-methylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-methylsulfonylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-cyanophenyl)-7-(4-(N-methyl-N-formylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-formylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-morpholinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methoxyethylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(dimethylamino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methoxyethyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-formyl-N-methyl amino)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(N-methylamino)5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-pyrrolidinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-(1-morpholinyl)-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-oxo-3-oxazolidinyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(thiophen-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(furan-2-yl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-(3-methoxyphenyl)phenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-(morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(thiophen-2-yl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(4-(5-pyrimidinyl)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromo-4-fluorophenyl)-7-(4-iodophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(4-bromothiophene-2-yl)-7-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-bromophenyl)methyl-7-(4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-phenylethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-methylpropyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(butyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(4-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(butyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(3-cyanophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(N-phenylmethoxycarbonyl)aminoethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(cycloheptyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(5-chloro-2-(thiophen-3-yl)phenylmethyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(pentyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-hexyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-((2-bromophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-cyclopropyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-cyclohexyl-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-((2-bromo-5-chlorophenyl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-methyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2,3-methylenedioxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3-fluoro-5-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(2-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,5-dimethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;
4-amino-5-(3,4-dichlorophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-fluoro-3-trifluoromethylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-morpholinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-piperidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylthiophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-5-methoxyphenyl)-7-(thiophene-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2,3-dimethoxyphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-methylsulfonylphenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-acetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(methoxyacetyl)amino-5-(3-bromophenyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-trifluoroacetylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-pentanoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-benzoylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-BOC-glycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(*N*-phthalimidylglycyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethoxycarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-(ethylaminocarbonyl)amino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-allylamino-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(2-(N,N-dimethylamino)ethylamino)-5-(4-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(4-(N,N-dimethylamino)butylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl) pyrido[2,3-d]pyrimidine;

4-(N-allyl-N-formylamino)-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-diacetylamino-5-(p-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-amino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-dimethylamino-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-2-oxobenzoxazolin-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-((5-chloro-2-(3-methoxyphenyl)phenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-2-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((thiophene-3-yl)methyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-formyl-N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-(2-methoxyethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-((2-dimethylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-methoxy)acetylamino)ethyl)amino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-((4-formylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)acetylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-oxo-3-oxazolidinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(2-propyl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-methyl-4-pyrrolidinylphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-phenylmethyl-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-(3-aminopropynyl)phenylmethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(3-bromophenyl)ethyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-dimethylaminophenyl)-7-(4-bromophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-furanyl)-7-(4-(N-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-dimethylamino-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(ureido)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-phenylmethyl-3-piperidinyl)-7-(4-diethylaminophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-methyl-5-isoxazolyl))-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-chloro-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-methoxy-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(1,2,4-triazol-4-yl)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-morpholinyl-5-pyrimidinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-thiazolyl)-7-(4-pyrrolidinylphenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrazolyl-3-pyridinyl))-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-ureido)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-(2-pyrimidinyl)amino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-formylamino-5-(3-bromophenyl)-7-(3-fluoro-4-(N-formyl-N-methylamino)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(N-methyl-N-methylsulfonylamino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-methylsulfonylamino)-3-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(1-methyl-5-benzimidazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3bromophenyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-pyrrolidinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-morpholinyl-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-(2-methoxyethyl)-N-methylamino)-2-pyrazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(morpholinylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N,N-bis(2-methoxyethyl)amino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(imidazolylmethyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-morpholinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((dimethylamino)methyl)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(4-hydroxy-1-piperidinyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(N-formyl-N-methylamino)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(2-propenyl)-2-pyridinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-(2-methoxyethyl)-2-oxo-6-benzoxazolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(N-formylamino)-ethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-(methylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-(2-methoxyethylamino)-5-(3-bromophenyl)-7-(4-dimethylaminophenyl)pyrido[2,3-d]pyrimidine hydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-2-imidazolyl)phenyl)pyrido[2,3-d]pyrimidine trihydrochloride;

4-amino-5-(3-bromophenyl)-7-(4-(aminomethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2-bromo-4-(dimethylamino)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(dimethylaminoethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(dimethylamino)propynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-amino-3-methylbutynyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-dimethylphosphonatophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(3-(methoxypropynyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-carboxyphenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(2-(dimethylamino)ethyl)-3-oxo-2H-4H-pyrido[3,2-b]-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,3-dihydro-3-(dimethylaminoethyl)-2-oxobenzoxazol-6-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-methyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(2,2,4-trimethyl-3-oxo-2H-4H-benzo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-(2-dimethylamino)ethyl)-2H-4H-benzo-3-oxo-1,4-oxazin-7-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-(1-methylethyl)-2-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-piperidin-1-ylpyrid-2-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(4-bromophenyl)ethyl)-7-(6-morpholinylpyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-((N-formylamino)methyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-methyl-1-(N-methylamino)ethyl)phenyl)-pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-(1-(dimethylamino)-1-methylethyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(N-acetyl-5-indolinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-diethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(4-(N-methyl-N-formyl)amino)-phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((2-bromophenyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-tetrahydropyranyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-ethylpropyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclopentyl-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(2-chloro-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3,5-dimethylcyclohexyl)-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-((N-(benzyloxycarbonyl)-4-piperidinyl)methyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-bromo-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(3-cyanophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-dimethylamino-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-imidazolyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(azacycloheptanyl)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-methyl-N-(1-methylethyl))amino)-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(6-morpholinyl-3-pyridazinyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-acetyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine:

4-amino-5-cyclohexyl-7-(6-(4-methyl-1,4-diazacycloheptanyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(2-(2-pyridyl)ethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-2-(N-(N',N'-dimethylaminoethyl)-N-methylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-azetidinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(N-methylacetamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(3-(formamido)pyrrolidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5[decan-8-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(2-methoxymethyl)pyrrolidin-1-yl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methoxyethyl-N-propylamino)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(2,2-dimethoxyethyl)amino)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(dimethylamino)piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-(aminocarbonyl))piperidinyl)pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(N-methyl-N-(3-(diethylamino)propyl)aminopyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(4-pyridyl)ethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(N-methyl-N-(3-pyridylmethylamino)pyrid-3-yl)pyrido[2,3-d]pyrimidine;

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-5-indolyl)pyrido[2,3-d]pyrimidine:

4-amino-5-(1-(2-bromophenyl)ethyl)-7-(1-methyl-2,3-dioxo-5-indolyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(3-fluoro-4-(1-morpholinyl)phenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-3-nitrophenyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-oxopiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-formylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4-methylpiperazinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-thiomorpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidin;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-dioxothiomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(2-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromo-4-methoxyphenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(4-bromophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-chlorophenyl)-7-(6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(5-chloro-6-morpholinyl-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-oxidomorpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)amino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-N-formylamino)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(N-(2-hydroxyethoxyethyl)-3-pyridyl-N-oxide)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(3-hydroxy)morpholinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

1-(5-(4-amino-5-(3-bromophenyl)pyrido[2,3-d]pyrimidin-7-yl)-2-pyridyl)-piperidine-4-phosphate, disodium salt;

4-amino-5-(3-bromophenyl)-7-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(4-hydroxy-4-(hydroxymethyl)piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-(3-bromophenyl)-7-(6-(4,4-ethylenedioxypiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

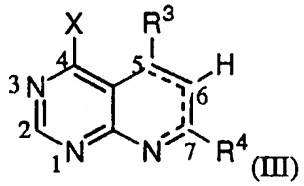
4-amino-5-cyclohexyl-7-(6-(4-oxo-piperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-amino-5-cyclohexyl-7-(6-(4-methylenylpiperidinyl)-3-pyridyl)pyrido[2,3-d]pyrimidine;

4-N-(iminomethyl)amino-5-cyclohexyl-7-(6-dimethylamino-3-pyridyl)pyrido[2,3-d]pyrimidine.

15. A pharmaceutical composition comprising a compound according to Claim 10 and a pharmaceutically acceptable carrier.

16. A compound of formula III

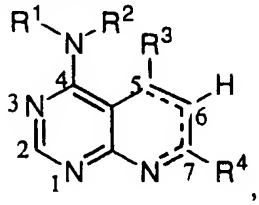


(III)

wherein X is selected from -OH or halogen and R^3 and R^4 are as defined above and a dashed line---indicates a double bond is optionally present.

17. A compound according to Claim 16 wherein said compound is an intermediate in a process to produce a compound according to Claim 10 or 11.

18. A process for the preparation of an adenosine kinase inhibiting compound having the formula

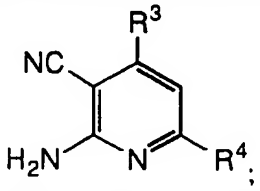


, (I) wherein R^1 and R^2 are hydrogen,

the method comprising

(a) reacting a ketone having the formula R^4-CO-CH_3, wherein R^4 is as defined above, with an aldehyde having the formula R^3-CHO, wherein R^3 is as defined above and malononitrile

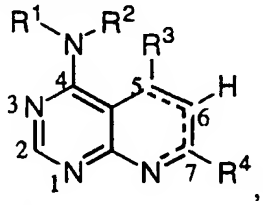
in the presence of an ammonium salt under anhydrous conditions and isolating a first intermediate compound having the structure



(b) reacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula (I) which has a double bond between the 5,6 carbons and a double bond between the 7 carbon and the 8 nitrogen and

(c) optionally reducing the compound from step (b) to form a partially reduced or fully reduced right side of formula I by catalytic hydrogenation.

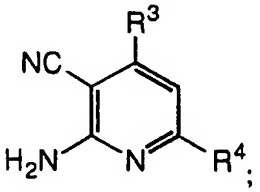
19. A process for the preparation of an adenosine kinase inhibiting compound having the formula



, (I) wherein R^1 and R^2 are hydrogen,

the method comprising

(a) reacting a ketone having the formula R^4-CO-CH_3, wherein R^4 is as defined above, with an dicyanoalkene compound having the formula R^3-CH=C$(CN)_2$, wherein R^3 is as defined above by heating at reflux and isolating a first intermediate compound having the structure



(b) reacting the first intermediate compound with formamide at reflux for from about 1 to about 8 hours, and isolating the compound of formula (I) which has a double bond between the 5,6 carbons and a double bond between the 7 carbon and the 8 nitrogen and

(c) optionally reducing the compound from step (b) to form a partially reduced or fully reduced right side of formula I by catalytic hydrogenation.

INTERNATIONAL SEARCH REPORT

Interr. ..al Application No
PCT/US 98/07207

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D471/04 A61K31/495

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 July 1998	07. 08. 98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fink, D

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INTERNATIONAL SEARCH REPORT

Interna .al Application No
PCT/US 98/07207

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 116, no. 9, 2 March 1992 Columbus, Ohio, US; abstract no. 083622, BAYOUMY B E ET AL: "New synthesis of pyridopyrimidine and pyridotetrahydroquinoline derivatives" page 816; column 1; XP002071948 see abstract & ZHONGHUA YAOXUE ZAZHI , vol. 43, no. 5, 1991, pages 365-371, see the abstract and the RN: [138744-57-7] = Pyrido[2,3-d]pyrimidin-4-amine, 7-(4-chlorophenyl)-5-phenyl; [138744-56-6] = Pyrido[2,3-d]pyrimidin-4-amine, 5,7-bis(4-chlorophenyl); [138744-55-5] = Pyridopyrimidine-4(1H)-one, 7-(4-chlorophenyl)-5-phenyl; [138744-54-4] = Pyrido[2,3-d]pyrimidin-4-(1H)-one, 5,7-bis(4-chlorophenyl); [69932-56-5] = Pyrido[2,3-d]pyrimidin-4(1H)-one, 5,7-diphenyl; ---	10-13,16
X	SWATI ET AL: "Synthesis and antimicrobial evaluation of some substituted pyrido[2,3-d]pyrimidines" INDIAN J. PHARM. SCI. , vol. 57, no. 6, 1995, pages 229-232, XP002071942 see page 231; the compounds IIIa - IIIc of the table ---	7,10-13, 15
X	SHARMA S A K ET AL: "Synthesis of some pyrido[2,3-d]pyrimidine derivatives and their antimicrobial activity" HETEROCYCL. COMMUN. , vol. 1, no. 1, 1994, pages 89-94, XP002071943 see pages 92-93, the compounds 6a and 6b in the tables 1 and 2 ---	7,10-13, 15
X	PRAKASH L ET AL: "Synthesis of some new 5,7-disubstituted pyrido[2,3-d]pyrimidine derivatives and their antibacterial activity" INDIAN J. HETEROCYCL. CHEM. , vol. 1, no. 1, 1991, pages 21-25, XP002071944 see page 23; the compounds IVa and IVb in table 1 --- -/--	7,10-13, 15

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INTERNATIONAL SEARCH REPORT

Interr. ..al Application No
PCT/US 98/07207

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DAVE C G ET AL: "Pyridopyrimidines: Part III. Synthesis and analgesic activity of 4-aminopyride[2,3-d]pyrimidines" INDIAN J. PHARM. SCI. , vol. 48, no. 3, 1986, pages 75-77, XP002071945 see page 76; the compounds IIb-IIe in table 1 ---	7,10-13, 15
X	ROBINS R K ET AL: "Studies on Condensed Pyrimidine Systems. XIX. A New Synthesis of Pyrido[2,3-d]pyrimidines. The Condensation of 1,3-Diketones and 3-Ketoaldehydes with 4-Aminopyrimidines" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 80, no. 13, 8 July 1958, DC US, pages 3449-3457, XP002071946 see page 3454; table V, the first entry ---	16
P,X	DAVE C G ET AL: "Diethyl ethoxymethylenemalonate in triheterocycles: a new synthesis of pyrido[3,2-e]pyrimido[1,2-c]pyrimidines" J. HETEROCYCL. CHEM. , vol. 34, no. 6, - November 1997 pages 1805-1808, XP002071947 see page 1806; scheme 2, the compound 2c ---	10-12
X	WO 95 19774 A (WARNER LAMBERT CO) 27 July 1995 cited in the application see page 161 - page 164; claim 71 see page 168 - page 171; claim 74 ---	7,10-15
A	WO 96 40686 A (ABBOTT LAB) 19 December 1996 see the whole document ---	1-15
A	WO 92 08456 A (AMIRA INC) 29 May 1992 see page 51, line 21 -----	1-15

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No
PCT/US 98/07207

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9519774 A	27-07-1995	US 5654307 A	05-08-1997
		AU 686334 B	05-02-1998
		AU 1731495 A	08-08-1995
		AU 686339 B	05-02-1998
		AU 1833495 A	08-08-1995
		BG 100614 A	31-03-1997
		BG 100615 A	28-02-1997
		CA 2177372 A	27-07-1995
		CA 2177392 A	27-07-1995
		CN 1139383 A	01-01-1997
		CN 1139430 A	01-01-1997
		CZ 9601970 A	17-09-1997
		CZ 9601971 A	16-07-1997
		EP 0742717 A	20-11-1996
		EP 0741711 A	13-11-1996
		FI 962855 A	13-09-1996
		FI 962856 A	25-09-1996
		HR 950033 A	31-10-1997
		HR 950034 A	31-10-1997
		HU 74590 A	28-01-1997
		HU 74589 A	28-01-1997
		JP 9508126 T	19-08-1997
		JP 9508127 T	19-08-1997
		NO 963093 A	24-07-1996
		NO 963094 A	24-07-1996
		PL 315632 A	25-11-1996
		PL 315633 A	25-11-1996
		SK 89496 A	08-10-1997
		SK 89596 A	06-08-1997
		WO 9519970 A	27-07-1995
		US 5679683 A	21-10-1997
		ZA 9500441 A	10-10-1995
		ZA 9500440 A	10-10-1995
WO 9640686 A	19-12-1996	NONE	
WO 9208456 A	29-05-1992	US 5324731 A	28-06-1994
		AU 1002497 A	20-03-1997
		AU 8948591 A	11-06-1992
		EP 0557383 A	01-09-1993

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inten nal Application No
PCT/US 98/07207

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9208456 A		JP 6506666 T	28-07-1994
		US 5676978 A	14-10-1997
		US 5321030 A	14-06-1994